RN: 7440-54-2

Barb

Access DB# 101008

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: P Spivack Examiner #: 70400 Date: 8/11/03
Art Unit: 1614 Phone Number 30 84703 Serial Number: 10/084,604
Mail Box and Bldg/Room Location: 2D01 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Preventing pressure-induced apoptotic neuronal cell death

Inventors (please provide full names): Coroneo Minas

Earliest Priority Filing Date: 8/29/00

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search methods for treating glaucoma comprising administering a gadolinium (Gd) a lanthanide to block stretch-activated channels of retinal ganglion to prevent retinal ganglia from apoptosis.

gadolinium = a rare earth metal

Please do inventor's search.

as part of NMR contrast medium); a diagnostic aid

Thanks

****

STAFF USE ONLY

Searcher: BOB

Searcher Phone #:

Searcher Location:

Date Searcher Picked Up:

Date Completed:

Searcher Prep & Review Time: 20

Clerical Prep Time:

Online Time: 57

Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#)

Bibliographic 1

Litigation

Fulltext

Patent Family

Other

Vendors and cost where applicable

STN 337

Dialog

Questel/Orbit

Dr.Link

Lexis/Nexis

Sequence Systems

WWW/Internet

Other (specify)

PTO-1590 (8-01)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 15:58:45 ON 12 AUG 2003
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:   11 AUG 2003  HIGHEST RN 565156-77-6
DICTIONARY FILE UPDATES:  11 AUG 2003  HIGHEST RN 565156-77-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> e gandolium/cn
E1            1     GANDHARAMINE CHLORIDE/CN
E2            1     GANDHARAMINE IODIDE/CN
E3            0 --> GANDOLIUM/CN
E4            1     GANEFROMYCIN .ALPHA./CN
E5            1     GANEFROMYCIN .ALPHA.1/CN
E6            1     GANEFROMYCIN .BETA./CN
E7            1     GANEFROMYCIN .BETA. AGLYCONE/CN
E8            1     GANEFROMYCIN .DELTA.1/CN
E9            1     GANEFROMYCIN .DELTA.2/CN
E10           1     GANEFROMYCIN .DELTA.3/CN
E11           1     GANEFROMYCIN .DELTA.4/CN
E12           1     GANEFROMYCIN .EPSILON./CN


=> stnindex
ENTER FILE OR CLUSTER NAMES (NONE):allbib
FILE 'ENCOMPLIT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT' ACCESS NOT AUTHORIZED
INDEX '1MOBILITY, 2MOBILITY, ADISCTI, AEROSPACE, AGRICOLA, ALUMINIUM, ANABSTR,
       APOLLIT, AQUASCI, AQUIRE, BABS, BIBLIODATA, BIOBUSINESS, BIOCOMMERCE,
       BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, CAOLD,
       CAPLUS, CASREACT, CBNB, CEABA-VTB, ...' ENTERED AT 15:59:01 ON 12 AUG 2003

131 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s gandolium
  57 FILES SEARCHED...
           5   FILE INVESTEXT
 111 FILES SEARCHED...
           1   FILE WPIDS
           1   FILE WPINDEX

   3 FILES HAVE ONE OR MORE ANSWERS,  131 FILES SEARCHED IN STNINDEX

L4    QUE GANDOLIUM
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=>
=> b hits
FILE 'INVESTEXT' ENTERED AT 16:00:21 ON 12 AUG 2003

FILE 'WPIDS' ENTERED AT 16:00:21 ON 12 AUG 2003

FILE 'WPINDEX' ACCESS NOT AUTHORIZED

=> s l4
L5 6 L4

=> d iall 1-6

L5 ANSWER 1 OF 6 INVESTEXT COPYRIGHT 2003 TFS on STN

Accession No.: 2003:904902 INVESTEXT(tm) REPORT NUMBER:8796955
Page No.: PAGE 8 OF 17
Document No.: 8796955
Title: BIOTECHNOLOGY - MARKETING BATTLE GETS HOTTER
Author: COPITHORNE, C.L., ET AL
Corp. Source: MORGAN STANLEY; NEW YORK (STATE OF)
Region: MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Publication Date: 24 Sep 2002
Report Type: INDUSTRY REPORT
File Segment: Text Page; INDUSTRY REPORT
Text Word Count: 702
Subject Heading: Perceived Disadvantages:

TEXT:

* Slower onset of action-Although it is difficult to compare data and determine the exact onset of action for each therapy, it appears Copaxone does not work as quickly as the high-does interferons (9 or more months for Copaxone versus 3-6 months for Rebif and Betaseron). In addition, physician feedback we received has depicted Copaxone's mechanism of action as "a bit slower", making it" more appropriate in lesssevere (still in relapsing remitting stage) patients".

Subject Heading: Future Steps:

TEXT:

Future Steps:
* Combination trials-The BEYOND study, a three arm, double-blinded study, with a duration of two years, should begin soon. This 2,000+ patient study will compare Betaferon (250 im) versus high-dose Betaferon (500 im) versus Copaxone (20mg sc daily). The primary endpoints are still under review by the steering committee, but will likely be either proportion of relapse-free patients or time to first relapse. Data is expected in 2005. In addition, a small trial was conducted using Avonex in combination with Copaxone, and demonstrated safety. However, efficacy of the Copaxone/interferon combination has not been studied in larger, controlledtrials to date.

Subject Heading: Data Coming out of ECTRIMS Meeting

TEXT:

Data Coming out of ECTRIMS Meeting

Though no new critical data came out of this year's ECTRIMS meeting, certain data presentations of particularinterest, are highlighted below.

Subject Heading: Biogen/Elan: More Details from Antegren Phase II Trial

TEXT:

Biogen/Elan: More Details from Antegren Phase II Trial
The Antegren Phase II trial data presented at last year's ECTRIMS meeting was overwhelmingly positive. The Street was very excited about the compound's prospects and doctors continue to be focused on the only late-stage MS therapy. Though the Phase IIb study overwhelmingly met its primary endpoint, a significant 88% reduction in brain lesions after 6 months, confirming Phase IIa trial results, we note that the secondary endpoint, EDSS score improvement, was not statistically significant. But, it is important to note that the trial was not powered to show a difference in EDSS and six months is a relatively short period of time in which to demonstrate benefit with regard to disability, despite Antegren's apparent rapid onset of action. Also, the placebo group declined only very slightly in the Phase IIb trial, thereby making it difficult to demonstrate Antegren's benefit with statistical significance. However, as that the Phase III Antegren trial is measuring EDSS score as a primary endpoint and given the clinical significance of the EDSS score and long-term nature of demonstrating differences in EDSS scores, we believe it will be difficult for Antegren to demonstrate a statistically significant improvement in EDSS at the one-year interim look. Exhibit 1 below highlights the Antegren Phase II EDSS data and theAvonex Phase III pivotal trial EDSS scores.

Table Title: Exhibit 1 EDSS Scores: Avonex Pivotal Trial and Antegren Phase II

TEXT:

Exhibit 1 EDSS Scores: Avonex Pivotal Trial and Antegren Phase II

	Placebo	Avonex(*)	Placebo	Antegren(**) 3mg/kg	Antegren(**) 6mg/kg
Mean Change in EDSS score from baseline	+0.50	+0.20	+0.03	-0.14	-0.03

(*) per Avonex label: Phase III pivotal trial results (p=0.006) (**) Phase IIb Antegren trial (not stat. sig.) Source: Company data, Morgan Stanley Research
As a reminder, Biogen and Elan (covered by Marc Goodman) are developing Antegren. The Phase IIb Antegren trial was a randomized, double-blinded, placebo-controlled 213-patient Phase IIb study in MS. The drug was administered once per month for six months (3mg/kg or 6mg/kg or placebo) to patients suffering from MS (68% of the patients had relapsing-remitting MS and the remaining 32% were secondary progressive MS patients). Treated patients demonstrated a highly statistically significant 88% mean reduction in new lesions, the primary endpoint, as measured by **gandolium** -enhanced MRI
scans (p<0.0001).
The mean number of new lesions over the six-month study period was 9.6 lesions in the placebo group, far greater than 1.2 in the 3mg/kg group and 0.6 in the 6mg/kg group. Interestingly, a difference in the number of new lesions between the arms was observed after only four weeks of treatment in both RRMS and SPMS patients, demonstrating the drug's rapid onset of action. Furthermore, MRI data presented at this year's meeting showed that Antegren-treated patients did not rebound, as was previously speculated, with patients' relapse rate returning to the same level (not higher) as the placebo group within a few months after treatment was stopped.
Moreover, the proportion of relapse-free patients was higher in both

Antegren treatment groups as compared to placebo (p = 0.03: p=0.041 in the 3mg/kg group and p=0.025 in the

L5 ANSWER 2 OF 6 INVESTEXT COPYRIGHT 2003 TFS on STN

Accession No.: 2003:875470 INVESTEXT(tm) REPORT NUMBER:8790970
Page No.: PAGE 2 OF 10
Document No.: 8790970
Title: BIOGEN INC.
Author: COPITHORNE, C.L., ET AL
Corp. Source: MORGAN STANLEY; NEW YORK (STATE OF)
Region: MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Publication Date: 19 Sep 2002
Report Type: COMPANY REPORT
File Segment: Text Page; COMPANY REPORT
Text Word Count: 748
Subject Heading: Summary and Investment Conclusion

TEXT:

Summary and Investment Conclusion
Yesterday kicked off Day One of the European and American Committees for Treatment and Research in Multiple Sclerosis (ECTRIMS & ACTRIMS) meeting, where new incremental Phase II data was presented for Biogen and partner, Elan's Antegren. Recall that very positive results were previously released at last year's ECTRIMS conference, showing that the trial met its primary endpoint, a statistically significant mean reduction in new lesions as measured by **gandolium**-enhanced MRI scans (p<0.0001). However, data on a
clinically important secondary endpoint, which we believe was presented for the first time yesterday, did not reach statistical significance. The Expanded Disability Status Scale (EDSS) score, did show a modestly positive trend. In addition, no dose response was observed in EDSS score.
While it is not unusual to fail to reach statistical significant in a Phase II trial, we find these results mildly disappointing given that data presented last year (on the primary endpoint of reduction in brain lesions) was so overwhelmingly positive. The lack of a convincing trend in this Phase IIb trial may be explained by the relatively short duration of the trial (only 6 months in duration versus 2-year studies used as the basis for other MS therapy approvals using EDSS scores), and, interestingly, the placebo group did not deteriorate significantly, making it more difficult for Antegren to show significant clinical benefit.
Thus, we find this data somewhat disappointing and believe that it may put the Antegren program at slightly higher risk since the ongoing Phase III trial's primary endpoint is the EDSS score (and not the reduction in new lesions on which Phase II data was overwhelmingly positive). Also, the clinical endpoints such as EDSS have been the focus for FDA approved MS drugs, rather than only surrogate endpoints (such as MRI-enhanced lesions). While the less compelling outcome in the secondary endpoint may be due to the very limited deterioration in the placebo group or the short duration of the trial, it incrementally reduces the visibility on the potential impact of Antegren on the primary endpoint in the Phase III.
Also, investigators at the Biogen/Elan-sponsored symposium announced that Phase III Antegren results would be announced in 2005, implying a filing in 1H 2005 at the earliest. This is later than our expectations, which were based on faster study enrollment (Phase III began in 4Q 2001), potential for expedited FDA review on positive interim one-year results, as discussed at the November 2001 analyst meeting. The company's long term forecast included an early 2005 Antegren launch and did not assume the trial would be halted early at the one year timepoint (of a two-year trial). The clinicians' expectation of data first becoming available in 2005, appears at odds with the assumed timeline of a 2005 launch -- potentially putting

the Antegren timeline at risk. We estimate Antegren sales of $150 million and $300 million in 2005 and 2006, respectively (on which Biogen splits profits 50/50 withElan), with limited erosion of Avonex sales assumed.

Subject Heading: Valuation and Risks

TEXT:

Valuation and Risks
Our price target is $36 and is based on a 1.2 multiple (near the lower-end of its historical range) on Biogen's long-term growth rate of 18% (2003-2006), on our 2003 estimate of $1.70. We remain on the sidelines as we view 2002 as a building year, and the longer-term outlook is still uncertain with a 5-year (2001-2006) CAGR of only 9% (3-year from 2003-2006 at 18%, but highly dependent on Amevive), far lower than the group average of 27%, even with continued modest growth of Avonex, ramp up of Amevive beginning in 2003, contribution of Humicade in 2004 and Antegren in 2005. Risks to our valuation and earnings estimates include regulatory risk surrounding the BLA resubmission and potential FDA approval of Amevive, clinical development risk of Humicade and Antegren, and slowing Avonex salesgrowth given increased competition in the MS market

Subject Heading: Phase II Results Good--But Not As Good as Last Year

TEXT:

Phase II Results Good But Not As Good as Last Year
The Antegren Phase II trial data presented at late year's ECTRIMS meeting was overwhelmingly positive. The Street was very excited about the compound's prospects and doctors continue to be focused on this, the only late-stage MS therapy. The Phase IIb study met its primary endpoint, a significant reduction in brain lesions after 6 months, confirming Phase IIa trial results. The secondary endpoint, EDSS score improvement, released yesterday was not statistically significant, however. It is important to note that the placebo group deteriorated only very slightly in the Phase IIb trial (related to what we have seen in other MS

Corporate Name & Codes:	BIOGEN INC. (Ticker Symbol: BGEN)
Address:	MASSACHUSETTS (COMMONWEALTH OF)
Region:	NEW ENGLAND/NORTHEAST REGION; UNITED STATES OF AMERICA; NORTH AMERICA

L5 ANSWER 3 OF 6 INVESTEXT COPYRIGHT 2003 TFS on STN

Accession No.:	2003:875469 INVESTEXT(tm) REPORT NUMBER:8790970
Page No.:	PAGE 3 OF 10
Document No.:	8790970
Title:	BIOGEN INC.
Author:	COPITHORNE, C.L., ET AL
Corp. Source:	MORGAN STANLEY; NEW YORK (STATE OF)
Region:	MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Publication Date:	19 Sep 2002
Report Type:	COMPANY REPORT
File Segment:	Text Page; COMPANY REPORT
Text Word Count:	780
Subject Heading:	Phase II Results Good--But Not As Good as Last Year

TEXT:

studies), and it may have been difficult to demonstrate Antegren's benefit with statistical significance. However, as that the Phase III Antegren

trial is measuring EDSS score as a primary endpoint and given the clinical significance of the EDSS score (versus surrogate markers like brain lesions), we have slightly reduced confidence in the outcome of the Antegren program achieving its primary endpoint. Exhibit 1 below highlights the Antegren EDSSdata and the Avonex pivotal trial EDSS scores.

Table Title: Exhibit 1 EDSS Scores: Avonex Pivotal Trial and Antegren Phase II

TEXT:

Exhibit 1 EDSS Scores: Avonex Pivotal Trial and Antegren Phase II

	Placebo	Avonex(*)	Placebo	Antegren(**) 3mg/kg	Antegren(**) 6mg/kg
Mean Change in EDSS score from baseline	+0.50	+0.20	+0.03	-0.14	-0.03

(*) per Avonex label: Phase III pivotal trial results (p=0.006) (**) Phase IIb Antegren trial (not stat. sig.) Source: Company data, Morgan Stanley Research

As a reminder, the Phase IIb Antegren trial was a randomized, double-blinded, placebo-controlled 213-patient Phase IIb study in MS. The drug was administered once per month for six months (3mg/kg or 6mg/kg or placebo) to patients suffering from MS (68% of the patients had relapsing-remitting MS and the remaining 32% were secondary progressive MS patients). Treated patients demonstrated a highly statistically significant, 88% mean reduction in new lesions, the primary endpoint, as measured by **gandolium**-enhanced MRI scans (p<0.0001). The mean number of new lesions over the six-month study period was 9.6 lesions in the placebo group, several fold greater than 1.2 in the 3mg/kg group and 0.6 in the 6mg/kg group. Interestingly, a difference in the number of new lesions between the arms was observed after only four weeks of treatment in both RRMS and SPMS patients (current MS therapies are only approved for RRMS with the exception of Betaseron in SPMS in Europe).

Moreover, the proportion of relapse-free patients was higher in both Antegren treatment groups as compared to placebo (p = 0.03: p=0.041 in the 3mg/kg group and p=0.025 in the 6 mg/kg group). Of the 71 patients in each group, the number of exacerbations was 34 in the placebo group and 19 and 14 in the two Antegren-treated groups with 3mg/kg and 6mg/kg, respectively. On a global measure of patient self-reported well being, Antegren-treated patients felt significantly better (p=0.03) than those treated with placebo. Antegren was considered safe and well tolerated; however, it should be noted that there were 4 patients with serious adverse events in the trial (3 cases of serum sickness -one in each arm of the trial and 1 case of an anaphylactic reaction).

Antegren, a humanized monoclonal antibody, is the first in the alpha 4 integrin inhibitor class of therapeutics, blocking cell adhesion to blood vessel walls and the subsequent migration of white blood cells into inflamed tissue. Its mechanism of action entails Antegren binding to alpha-4-beta-1 (VLA-4) surface receptors, which are found on most white blood cells. Biogen licensed Antegren from Elan in August 2000 and is obligated to pay Elan certain milestonepayments and royalties on future sales.

Subject Heading: Phase III Monotherapy Trial Enrolled and Combo Trial Almost Fully Recruited

TEXT:

Phase III Monotherapy Trial Enrolled and Combo Trial Almost Fully Recruited

At the meeting, we learned that the Phase III Antegren monotherapy trial is

now fully enrolled, with the last patient dose expected in 2H 2004. The combination Phase III study (with Avonex) is also almost fully recruited. Thus, we expect full data from the comprehensive Phase III program in late 2004/early 2005. This timing is later than our previous assumptions, which were based on faster enrollment and the potential for approval based on one-year data (given the overwhelming and rapid benefit seen in previously presented Phase IIb data). However, if interim one-year data becomes the basis for approval, as was the case for Avonex, we would expect a BLA filing in early 2004 and approval in 2005.
In partnership with Elan, three Phase III Antegren trials are ongoing: 1) a monotherapy MS study, 2) Antegren in combination with Avonex in MS, and 3) a monotherapy trial in Crohns disease.
The Phase III MS trial is designed with an interim analysis at one year and, if interim results are positive, Antegren may be accelerated through the regulatory process. We expect one year interim results in 2H 2003 for the monotherapy trial and 1H 2004 for the combination trial (as enrollment is currently ongoing) with approval expected in 2005.
The monotherapy trial compares Antegren to placebo in relapsing remitting MS patients over two years (one-year interim look), measuring relapse rate, primary endpoint of Expanded Disability Severity Scale (EDSS) score and MRI lesions, relapses and MSFC scores (secondary endpoints). The combination study adds Antegren (IV) to interferon therapy in patients who have been on interferon treatment for over one year but with at least one documented relapse and utilizes the same endpoints as in the monotherapy trial.

Corporate Name & Codes:	BIOGEN INC. (Ticker Symbol: BGEN)
Address:	MASSACHUSETTS (COMMONWEALTH OF)
Region:	NEW ENGLAND/NORTHEAST REGION; UNITED STATES OF AMERICA; NORTH AMERICA

L5 ANSWER 4 OF 6 INVESTEXT COPYRIGHT 2003 TFS on STN

Accession No.:	2003:343181 INVESTEXT(tm) REPORT NUMBER:8482314
Page No.:	PAGE 7 OF 16
Document No.:	8482314
Title:	BIOTECH PRODUCTS- THE MS BATTLE: COMIN' OUT SWINGING
Author:	COPITHORNE, C.L., ET AL
Corp. Source:	MORGAN STANLEY, DEAN WITTER; NEW YORK (STATE OF)
Region:	MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Corp. So. Type:	Financial center investment bank-broker
Publication Date:	17 Apr 2002
Report Type:	INDUSTRY REPORT
File Segment:	Text Page; INDUSTRY REPORT
Text Word Count:	392
Subject Heading:	Antegren Still Impressing Doctors

TEXT:

Recall that the randomized, double-blinded, placebo-controlled 213-patient Phase IIb Antegren study in MS achieved its primary endpoint, a significant reduction in brain lesions after 6 months, confirming Phase IIa trial results. Antegren was administered once per month for six months (3mg/kg or 6mg/kg or placebo) to patients suffering from MS (68% of the patients had relapsing-remitting MS and the remaining 32% were secondary progressive MS patients). Treated patients demonstrated a highly statistically significant 88% mean reduction in new lesions as measured by **gandolium**-enhanced MRI scans ($p<0.0001$). The mean number of new lesions over the six-month study period was 9.6 lesions in the placebo group, far greater than 1.2 in the 3mg/kg group and 0.6 in the 6mg/kg group. Interestingly, a difference in the number of new lesions between the arms was observed

after only four weeks of treatment in both RRMS and SPMS patients (current MS therapies are only approved for RRMS with the exception of Betaseron in SPMS in Europe).

At the AAN meeting, additional data were presented for the first time. Most noteworthy of the various evaluations was the number of active MRI scans. About 39% of the placebo group had active scans versus only 9% and 11% in the 3 mg/kg and 6 mg/kg groups, respectively ($p<0.0001$). Given that audience members purposely stayed just for this presentation (a part of a larger MS session which included very early stage trials and small combination trials) despite the fact that it has already been presented at a major medical conference speaks volumes about the promise the MS community believes Antegren holds, in our view.

Table Title: Exhibit 1 Biogen Annual Income Statement 2001-06

TEXT:

Exhibit 1
Biogen Annual Income Statement

(Part 1 of 4)

($ in thousands,
except per share data)

	2001	% Chg.	2002E
Revenues			
Avonex- US	711,077	28.9%	776,710
Avonex-Europe	260,542	24.5%	321,625
Amevive	-		
Antegren	-		-
Royalties	71,766	-56.6%	80,000
Total Revenues	1,043,386	12.6%	1,178,335
Cost Of Sales	136,510	9.0%	155,540
R&D	306,556	1.2%	376,000
Selling, General & Admin.	232,096	36.5%	320,000
Other	-	NM	-
Total Operating Expenses	675,162	12.9%	851,540
Net Operating Income	368,224	12.1%	326,795
Interest Income	29,299	-81.5%	51,608
Pretax Income (Loss)	397,523	-18.4%	378,403
Income Tax	119,231	-22.3%	105,953
Tax Rate	30.0%		28.0%
Net Operating Income	278,291	-16.6%	272,450
Write-Off -- After Tax			
EPS -- From Operations	$1.91	9.2%	$1.78
EPS -- Net	$1.78	-17.4%	$1.78
Shares Outstanding Diluted	152,916	-1.1%	152,884

Controlled Term: INTERNATIONAL SALES/MARKETING; SALES BY PRODUCT/SALES BY PRODUCT LINE; RESEARCH AND DEVELOPMENT; MARKET SIZE/DEMOGRAPHICS; COMPANY ANALYSES; ANNUAL/OPERATING RESULTS; SALES/EARNINGS; EARNINGS PER SHARE; PROJECTIONS

L5 ANSWER 5 OF 6 INVESTEXT COPYRIGHT 2003 TFS on STN

Accession No.: 2002:828776 INVESTEXT(tm) REPORT NUMBER:8177508
Page No.: PAGE 3 OF 5
Document No.: 8177508
Title: ELAN CORPORATION PLC

Author: GOODMAN, M.
Corp. Source: MORGAN STANLEY, DEAN WITTER; NEW YORK (STATE OF)
Region: MID-ATLANTIC/MIDDLE ATLANTIC REGION; UNITED STATES OF AMERICA; NORTH AMERICA
Corp. So. Type: Financial center investment bank-broker
Publication Date: 17 Sep 2001
Report Type: COMPANY REPORT
File Segment: Text Page; COMPANY REPORT
Text Word Count: 525
Subject Heading: Summary and Investment Conclusion

TEXT:

At this time, we are making no changes to our Antegren sales forecast of $40 million in 2006, which appears conservative until we are able to follow up with more physicians. Elan believes Antegren could be its first $1 billion product, and we don't rule this out. Notably, we currently have a $500 million placeholder in our model for Other Product sales in 2006, which reflects new products that Elan would need to acquire or develop internally in order to just achieve our estimated 16% EPS growth rate for the 2001-2006 period. We will be reviewing our MS market model, and some of the revenue forecasted for Other Products may potentially be shifted over to Antegren.

We are also making no changes to our EPS estimates of $1.94 ($1.42 excluding licensing revenues) for 2001 and $2.34 ($1.83 excluding licensing revenues) for 2002. Weremain Neutral on the stock.

Subject Heading: Phase II MS Study Details

TEXT:

Phase II MS Study Details

The randomized, double-blinded, placebo-controlled 213-patient Phase IIb Antegren study in MS achieved its primary endpoint, a significant reduction in brain lesions after 6 months, confirming Phase IIa trial results. Antegren was administered once per month for six months (3mg/kg or 6mg/kg or placebo) to patients suffering from MS (68% of the patients had relapsing-remitting MS and the remaining 32% were secondary progressive MS patients). Treated patients demonstrated a highly statistically significant 88% mean reduction in new lesions as measured by **gandolium**-enhanced MRI scans ($p<0.0001$). The mean number of new lesions over the six-month study period was 9.6 lesions in the placebo group, far greater than 1.2 in the 3mg/kg group and 0.6 in the 6mg/kg group. Interestingly, a difference in the number of new lesions between the arms was observed after only four weeks of treatment in both RRMS and SPMS patients. Current MS therapies are only approved for RRMS with the exception of Betaseron in SPMS in Europe. We estimate that about 80% of MS therapies are used for RRMS and 20% for SPMS. Thus, there is potential for Antegren to further expand the MS market by increasing the number of SPMS patients that will receive treatment.

The proportion of relapse-free patients was higher in both Antegren treatment groups as compared to placebo ($p = 0.03$: $p=0.041$ in the 3mg/kg group and $p=0.025$ in the 6 mg/kg group). Of the 71 patients in each group, the number of exacerbations was 34 in the placebo group and 19 and 14 in the two Antegren-treated groups with 3mg/kg and 6mg/kg, respectively. On a global measure of patient self-reported well-being, Antegren-treated patients felt significantly better ($p=0.03$) than those treated with placebo. Antegren was considered safe and well tolerated; however, it should be noted that there were 4 patients with serious adverse events in the trial (3 cases of serum

sickness -one in each arm of the trial and 1 case of an anaphylactic reaction). Phase III studies are expected to begin in the 4Q (as both a monotherapy and in combination with Avonex), and we believe that the adverse events seen in the Phase II trial will be watched carefully. We have not heard yet what the protocol will be for the Phase III study.

Corporate Name & Codes: ELAN CORP., PLC ADS (Ticker Symbol: ELN)
Address: IRELAND (REPUBLIC OF)
Region: WESTERN EUROPE REGION; EUROPE
Controlled Term: SALES BY PRODUCT/SALES BY PRODUCT LINE; RESEARCH AND DEVELOPMENT; NEW PRODUCTS/SERVICES; VALUATION; INVESTMENT RECOMMENDATION; EARNINGS PER SHARE; PROJECTIONS
Product Desc.: NEUROLOGICAL DRUGS
SIC Code: 2834
CC BIOTEC BIOTECHNOLOGY; PHARMS PHARMACEUTICALS

L5 ANSWER 6 OF 6 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1992-213986 [26] WPIDS
DOC. NO. NON-CPI: N1992-162487
DOC. NO. CPI: C1992-096885
TITLE: Improved quality photomagnetic recording medium - comprises recording layer of alloys contg. at least one heavy rare earth metal and at least one of palladium , platinium and cobalt layers on substrate.
DERWENT CLASS: G06 L03 M26 T03 V02 W04
PATENT ASSIGNEE(S): (SHIH) SEIKO EPSON CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
JP 04143947	A	19920518	(199226)*		10	G11B011-10

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 04143947	A	JP 1990-267606	19901005

PRIORITY APPLN. INFO: JP 1990-267606 19901005
INT. PATENT CLASSIF.:
MAIN: G11B011-10
SECONDARY: G11B007-24
BASIC ABSTRACT:
JP 04143947 A UPAB: 19931006
Medium comprises the substrate and the recording layer formed on the substrate. The recording layer is composed of layers made of alloys contg. at least one kind of metal selected from the gp. consisting of the heavy rare earth metals, e.g. Gd, Tb and Dy, and at least one kind selected from the gp. consisting of Pt and Pd and Co layers put one upon another.
Pref. the PtGd-Co alloys contg. Gd in the quantity of 5-60 at.% are used.
USE/ADVANTAGE - For the photomagnetic recording medium the satd. magnetisation of the recording layer can be reduced and thus the quality can be improved.
1/19
FILE SEGMENT: CPI EPI
FIELD AVAILABILITY: AB; GI
MANUAL CODES: CPI: G02-A05B; G06-C06; G06-D07; G06-F04; L03-B05F; M26-B
EPI: T03-D01A5; V02-A01A2; V02-B01; W04-D01A

```
=> fil reg; d ide l6
FILE 'REGISTRY' ENTERED AT 16:03:03 ON 12 AUG 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   11 AUG 2003  HIGHEST RN 565156-77-6
DICTIONARY FILE UPDATES:  11 AUG 2003  HIGHEST RN 565156-77-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L6   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   7440-54-2  REGISTRY
CN   Gadolinium (8CI, 9CI)  (CA INDEX NAME)
DR   87677-94-9, 110123-54-1
MF   Gd                          remember this is what I searched
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
       CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,
       CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, ENCOMPLIT,
       ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
       MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, TULSA,
       ULIDAT, USPAT2, USPATFULL, VTB
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)


Gd

          22882 REFERENCES IN FILE CA (1947 TO DATE)
           2718 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          22912 REFERENCES IN FILE CAPLUS (1947 TO DATE)


=> fil capl; d que l3; d que l8
FILE 'CAPLUS' ENTERED AT 16:47:50 ON 12 AUG 2003
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```

FILE COVERS 1907 - 12 Aug 2003 VOL 139 ISS 7
FILE LAST UPDATED: 11 Aug 2003 (20030811/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L2 20 SEA FILE=CAPLUS ABB=ON CORONEO M?/AU
L3 2 SEA FILE=CAPLUS ABB=ON APOPTO?/TI AND L2

L2 20 SEA FILE=CAPLUS ABB=ON CORONEO M?/AU
L6 1 SEA FILE=REGISTRY ABB=ON GADOLINIUM/CN
L7 22915 SEA FILE=CAPLUS ABB=ON L6
L8 1 SEA FILE=CAPLUS ABB=ON L2 AND L7

=> s l3 or l8

L127 2 L3 OR L8

=> fil medl; d que l37

FILE 'MEDLINE' ENTERED AT 16:47:51 ON 12 AUG 2003

FILE LAST UPDATED: 9 AUG 2003 (20030809/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L27 4252 SEA FILE=MEDLINE ABB=ON GADOLINIUM/CT
L28 69 SEA FILE=MEDLINE ABB=ON CORONEO M?/AU
L31 25217 SEA FILE=MEDLINE ABB=ON OCULAR HYPERTENSION+NT/CT
L33 454 SEA FILE=MEDLINE ABB=ON STRETCH(W)(ACTIVAT? OR INDUC?)(3A)CHANNEL#
L34 66112 SEA FILE=MEDLINE ABB=ON ION CHANNELS+NT/CT
L37 6 SEA FILE=MEDLINE ABB=ON L28 AND (L27 OR L31 OR (L33 AND L34))

=> fil embase; d que l63

FILE 'EMBASE' ENTERED AT 16:47:51 ON 12 AUG 2003

FILE COVERS 1974 TO 10 Aug 2003 (20030810/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L52          69 SEA FILE=EMBASE ABB=ON  CORONEO M?/AU
L53        4196 SEA FILE=EMBASE ABB=ON  GADOLINIUM/CT
L54       22630 SEA FILE=EMBASE ABB=ON  GLAUCOMA+NT/CT
L55       12278 SEA FILE=EMBASE ABB=ON  INTRAOCULAR PRESSURE/CT
L56        4805 SEA FILE=EMBASE ABB=ON  INTRAOCULAR PRESSURE ABNORMALITY+NT/CT

L62         344 SEA FILE=EMBASE ABB=ON  GADOLINIUM CHLORIDE/CT
L63           7 SEA FILE=EMBASE ABB=ON  L52 AND (L53 OR L62 OR L54 OR L55 OR
                L56)
```

```
=> fil wpids; d que l82

FILE 'WPIDS' ENTERED AT 16:47:52 ON 12 AUG 2003
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FILE LAST UPDATED:          8 AUG 2003      <20030808/UP>
MOST RECENT DERWENT UPDATE:     200351        <200351/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L74        7836 SEA FILE=WPIDS ABB=ON  GADOLINIUM OR GD
L75        4534 SEA FILE=WPIDS ABB=ON  ?GLAUCOMA?
L81           3 SEA FILE=WPIDS ABB=ON  CORONEO M?/AU
L82           2 SEA FILE=WPIDS ABB=ON  L81 AND ((L74 OR L75))


=> fil drugu; d que l91

FILE 'DRUGU' ENTERED AT 16:47:53 ON 12 AUG 2003
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FILE LAST UPDATED: 7 AUG 2003       <20030807/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<
```

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L91             3 SEA FILE=DRUGU ABB=ON  CORONEO M?/AU

=> fil biosis; d que l120

FILE 'BIOSIS' ENTERED AT 16:47:55 ON 12 AUG 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 6 August 2003 (20030806/ED)


L112            70 SEA FILE=BIOSIS ABB=ON  CORONEO M?/AU
L113         10064 SEA FILE=BIOSIS ABB=ON  GADOLINIUM OR GD
L114         22206 SEA FILE=BIOSIS ABB=ON  ?GLAUCOMA?
L120            12 SEA FILE=BIOSIS ABB=ON  L112 AND (L113 OR L114)


=> dup rem l37,l91,l123,l20,l63,l82

FILE 'MEDLINE' ENTERED AT 16:47:56 ON 12 AUG 2003

FILE 'DRUGU' ENTERED AT 16:47:56 ON 12 AUG 2003
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FILE 'CAPLUS' ENTERED AT 16:47:56 ON 12 AUG 2003
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PROCESSING COMPLETED FOR L37
PROCESSING COMPLETED FOR L91
PROCESSING COMPLETED FOR L123
PROCESSING COMPLETED FOR L20
PROCESSING COMPLETED FOR L63
PROCESSING COMPLETED FOR L82
L128            16 DUP REM L37 L91 L123 L20 L63 L82 (7 DUPLICATES REMOVED)
                   ANSWERS '1-6' FROM FILE MEDLINE
                   ANSWERS '7-8' FROM FILE DRUGU
                   ANSWERS '9-11' FROM FILE CAPLUS
                   ANSWERS '12-15' FROM FILE EMBASE
                   ANSWER '16' FROM FILE WPIDS

=> d ibib ab hitrn 1-16


L128 ANSWER 1 OF 16     MEDLINE on STN                    DUPLICATE 2
ACCESSION NUMBER:    2002630463     MEDLINE
DOCUMENT NUMBER:     22276096   PubMed ID: 12388044
TITLE:               Acute haptic-induced pigmentary glaucoma with an AcrySof
                     intraocular lens.
AUTHOR:              Micheli Tasha; Cheung Leanne M; Sharma Shanel; Assaad Nagi
```

N; Guzowski Magdalena; Francis Ian C; Norman Jenny; **Coroneo Minas T**

CORPORATE SOURCE: Ophthalmic Surgery Centre, University of New South Wales, Sydney, Australia.

SOURCE: JOURNAL OF CATARACT AND REFRACTIVE SURGERY, (2002 Oct) 28 (10) 1869-72.
Journal code: 8604171. ISSN: 0886-3350.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021022
Last Updated on STN: 20021217
Entered Medline: 20021212

AB A 49-year-old man had uneventful endocapsular phacoemulsification with in-the-bag implantation of an AcrySof SA60AT single-piece intraocular lens (IOL) (Alcon) in the right eye. Twenty-seven days postoperatively, he presented with ocular pain, intraocular pressure of 48 mm Hg, 360 degrees of hyperpigmentation of the trabecular meshwork, and iris pigment epithelial atrophy in the region of the upper temporal haptic, which had dislocated into the sulcus. The patient made an excellent recovery following IOL removal and exchange. Scanning electron microscopy of the explanted IOL demonstrated that the haptic had a rough lateral surface and anterolateral edge. We do not think this IOL should be implanted in the sulcus placement of the heptics. In this article, we report the case of a patient with an AcrySof SA60ATIOL (Alcon) who developed acute pigmentary glaucoma when the inferior haptic slipped out of the bag and came into contact with the pigmented iris and ciliary body.

L128 ANSWER 2 OF 16 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2000429676 MEDLINE
DOCUMENT NUMBER: 20406081 PubMed ID: 10946192

TITLE: Primary phacoemulsification for uncontrolled angle-closure glaucoma.

COMMENT: Comment in: J Cataract Refract Surg. 2000 Jul;26(7):941-2
Comment in: J Cataract Refract Surg. 2001 Feb;27(2):176-7

AUTHOR: Roberts T V; Francis I C; Lertusumitkul S; Kappagoda M B; **Coroneo M T**

CORPORATE SOURCE: The Eye Institute, Sydney, Australia.. troberts@theeyeinstitute.com.au

SOURCE: JOURNAL OF CATARACT AND REFRACTIVE SURGERY, (2000 Jul) 26 (7) 1012-6.
Journal code: 8604171. ISSN: 0886-3350.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20020319
Entered Medline: 20000911

AB PURPOSE: To report the results of primary phacoemulsification to treat uncontrolled angle-closure glaucoma. SETTING: Private practice and teaching hospital department. METHODS: This retrospective interventional case series assessed 3 patients having phacoemulsification and posterior chamber intraocular lens implantation for uncontrolled intraocular pressure (IOP) after acute primary angle-closure glaucoma. RESULTS: Intraocular pressure control was achieved in all patients postoperatively. CONCLUSIONS: Primary phacoemulsification with the option of future trabeculectomy should be considered in selected patients with persistent appositional angle closure and uncontrolled IOP after angle-closure glaucoma.

L128 ANSWER 3 OF 16 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2000259593 MEDLINE
DOCUMENT NUMBER: 20259593 PubMed ID: 10797552
TITLE: Pressure related apoptosis in neuronal cell lines.
AUTHOR: Agar A; Yip S S; Hill M A; **Coroneo M T**
CORPORATE SOURCE: Cell Biology Lab, School of Anatomy, University of New South Wales, Sydney, Australia.
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, (2000 May 15) 60 (4) 495-503.
Journal code: 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706
Entered Medline: 20000623

AB Pressure is a crucial component of the cellular environment, and can lead to pathology if it varies beyond its normal range. The increased intra-ocular pressures in acute glaucoma are associated with the loss of neurons by apoptosis. Little is known regarding the interaction between pressure and apoptosis at the level of the cell. The model developed in this study examines the effects of elevated ambient hydrostatic pressure directly upon cultured neuronal lines. Conditions were selected to be within physiological limits: 100 mmHg over and above atmospheric pressure for a period of 2 hr, as seen clinically in acute glaucoma. This system can be used to investigate pressure relatively independently of other variables. Neuronal cell line cultures (B35 and PC12) were subjected to pressure conditions in specially designed pressure chambers. Controls were treated identically, except for the application of pressure, and positive controls were treated with a known apoptotic stimulus. Apoptosis was detected by cell morphology changes and by 2 specific apoptotic markers: TUNEL (Terminal transferase dUTP Nick-End Labeling) and Annexin V. These fluorescent markers were detected and quantified by automated Laser Scanning Cytometry. All techniques showed that increased pressure was associated with a greater level of apoptosis compared to equivalent controls. Our results suggest that pressure alone may act as a stimulus for apoptosis in neuronal cell cultures. This raises the possibility of a more direct relationship at the cellular level between pressure and neuronal loss.

L128 ANSWER 4 OF 16 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 85163160 MEDLINE
DOCUMENT NUMBER: 85163160 PubMed ID: 3982353
TITLE: An eye for cricket. Ocular injuries in indoor cricketers.
AUTHOR: **Coroneo M T**
SOURCE: MEDICAL JOURNAL OF AUSTRALIA, (1985 Apr 15) 142 (8) 469-71.
Journal code: 0400714. ISSN: 0025-729X.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198505
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850523

AB Indoor cricket has become a popular form of recreation in Australia. Four cases of significant ocular trauma in indoor cricketers are reported. Three of the patients had diminished visual acuity in at least one eye before their injury. One patient may suffer long-term consequences as a

result of his injuries. These injuries could probably have been prevented by the use of appropriate eye protection. Indoor cricketers might well be advised to undergo ocular assessment before taking up this sport.

L128 ANSWER 5 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2002651151 MEDLINE
DOCUMENT NUMBER: 22273910 PubMed ID: 12386096
TITLE: Acute angle closure glaucoma following the use of intranasal cocaine during dacryocystorhinostomy.
AUTHOR: Wilcsek G A; Vose M J; Francis I C; Sharma S; **Coroneo M T**
SOURCE: BRITISH JOURNAL OF OPHTHALMOLOGY, (2002 Nov) 86 (11) 1312. Journal code: 0421041. ISSN: 0007-1161.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021105
Last Updated on STN: 20021218
Entered Medline: 20021213

L128 ANSWER 6 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2002454403 MEDLINE
DOCUMENT NUMBER: 22199710 PubMed ID: 12208694
TITLE: Trabeculectomy and angle closure.
COMMENT: Comment on: Ophthalmology. 2001 Jun;108(6):1008
AUTHOR: Roberts Tim; Francis Ian; Lertusumitkul Sam; Kappagoda Medduma; **Coroneo Minas**
SOURCE: OPHTHALMOLOGY, (2002 Sep) 109 (9) 1584-5. Journal code: 7802443. ISSN: 0161-6420.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020906
Last Updated on STN: 20020920
Entered Medline: 20020919

L128 ANSWER 7 OF 16 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1995-00099 DRUGU T M
TITLE: Ganciclovir intraocular device and patient survival.
AUTHOR: Morlet N; Young S H; **Coroneo M T**
LOCATION: Sydney, Austr.
SOURCE: Arch.Ophthalmol. (112, No. 11, 1404, 1994) 7 Ref.
CODEN: AROPAW ISSN: 0003-9950
AVAIL. OF DOC.: No Reprint Address.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB It is reported in a letter that intravitreal ganciclovir (2 mg/0.1 ml/wk) was effective in the treatment of 35 eyes in 22 patients with CMV-retinitis. An initial 100% response rate was seen and retinitis reoccurred in 6/35 (17%) eyes. Survival time in the patients (30 wk) compared favorable with survival from previous studies with i.v. ganciclovir. 6/12 Patients with unilateral disease treated with intravitreal ganciclovir developed disease in the 2nd eye, which again compared favorably with results from previous studies. Local therapy offers good control of CMV-retinitis without adversely risking survival or systemic side-effects compared with i.v. administration. (No EX).

L128 ANSWER 8 OF 16 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1992-50494 DRUGU M T S
TITLE: High Dose Intravitreal Ganciclovir in the Treatment of Cytomegalovirus Retinitis.
AUTHOR: Young S H; Morlet N; Heery S; Hollows F C; **Coroneo M T**
LOCATION: Sydney, Australia
SOURCE: Med.J.Aust. (157, No. 6, 370-373, 1992) 3 Tab. 36 Ref.
CODEN: MJAUAJ ISSN: 0025-729X
AVAIL. OF DOC.: Department of Ophthalmology, Prince of Wales Hospital, High Street, Randwick, NSW 2031, Australia.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB Treatment with high dose intravitreal (IVt) ganciclovir (GC) alone or combined with i.v. GC effectively suppressed CMV retinitis in a retrospective study of 23 AIDS patients with CMV retinitis (37 affected eyes). Relapse or loss of vision frequently occurred following treatment with i.v. GC alone or combined with intermittent IVt GC. The eyes were anesthetized with topical cocaine and chloramphenicol eye drops were given prophylactically. Side-effects were neutropenia, septicemia and axillary vein thrombosis with i.v. GC; subfoveal hemorrhage and endophthalmitis, due to Staph. epidermidis, with IVt GC. High dose IVt GC can suppress CMV retinitis and preserve vision without adverse systemic effects or deterioration of quality of life.

L128 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:122800 CAPLUS
DOCUMENT NUMBER: 136:161387
TITLE: Methods and compositions for preventing pressure-induced **apoptotic** neural cell death
INVENTOR(S): **Coroneo, Minas Theodore**
PATENT ASSIGNEE(S): Australia
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011739	A1	20020214	WO 2001-AU971	20010808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001078306	A5	20020218	AU 2001-78306	20010808
US 2002187919	A1	20021212	US 2002-84604	20020227

PRIORITY APPLN. INFO.:
AU 2000-9267 A 20000808
US 2000-649643 B1 20000829
WO 2001-AU971 W 20010808

AB Methods for protecting neural tissue from pressure-induced apoptotic cell death are provided which comprise administering at least one compd. (e.g. gadolinium or a gadolinium agonist) which blocks the effect of pressure on neuronal cells.

IT **7440-54-2**, Gadolinium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and gadolinium agonists; pressure-induced apoptotic neural cell death prevention)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:493550 CAPLUS
DOCUMENT NUMBER: 133:101736
TITLE: A reagent system and method for increasing the luminescence of lanthanide(iii) macrocyclic complexes
INVENTOR(S): Leif, Robert C.; Vallarino, Lidia
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042048	A1	20000720	WO 2000-US1211	20000118
W: CA, CH, DE, FI, GB, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2360054	AA	20000720	CA 2000-2360054	20000118
EP 1150985	A1	20011107	EP 2000-905653	20000118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6340744	B1	20020122	US 2000-484670	20000118
US 2002132992	A1	20020919	US 2001-10597	20011206

PRIORITY APPLN. INFO.: US 1999-116316P P 19990119
US 2000-484670 A1 20000118
WO 2000-US1211 W 20000118
OTHER SOURCE(S): MARPAT 133:101736
AB Disclosed are a spectrofluorimetrically detectable luminescent compn. and processes for enhancing the luminescence of one or more lanthanide-contg. macrocycles. The luminescent compn. comprises a micelle-producing amt. of at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compd. having an emission spectrum peak in the range from 500 to 950 nm, and a luminescence-enhancing amt. of at least one energy transfer donor compd. of yttrium or a 3-valent lanthanide element having at. no. 59-71, provided that the lanthanide element of said macrocycle compd. and the lanthanide element of said energy transfer donor compd. are not identical. The addn. of gadolinium(III) in the presence of other solutes to both the prototype and the difunctionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patents #5,373,093 and #5,696,240, enhances their luminescence. Similar enhancements of luminescence also results for the mono-functionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patent #5,696,240. The enhanced luminescence afforded by the compn. enables the detection and/or quantitation of many analytes in low concns. without the use of expensive, complicated time-gated detection systems.
IT **7440-54-2**, Gadolinium, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reagent system and method for increasing luminescence of lanthanide(iii) macrocyclic complexes)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L128 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:588649 CAPLUS
DOCUMENT NUMBER: 117:188649
TITLE: Divalent cation effects on lens conductance and **stretch-activated** cation **channels**
AUTHOR(S): Rae, James L.; Mathias, Richard T.; Cooper, Kim; Baldo, George
CORPORATE SOURCE: Dep. Physiol., Mayo Found., Rochester, MN, 55905, USA
SOURCE: Experimental Eye Research (1992), 55(1), 135-44
CODEN: EXERA6; ISSN: 0014-4835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In patch clamp studies of apical membrane from frog lens epithelium, the most frequently obsd. **channel** is **stretch-activated**, highly selective for cations over anions but showing little selectivity for Na+ vs. K+. In normal physiol. saline, the open channel conductance is 25-30 pS and quite linear over .+-. 100 mV. In the absence of extracellular divalent ions, the open channel conductance for inward current flow increases to about 50 pS at the normal lens resting voltage of -75 mV, whereas the conductance for outward current flow is unaffected. In the intact lens, removal of extracellular divalents causes the input conductance approx. to double and the intracellular voltage to depolarize from -74 to -58 mV. A variety of divalent ions block this change in whole lens conductance and voltage in the same order in which they block the stretch channels. Single voltage-clamped epithelial cells also increase their conductance when Ca2+ is removed from their bathing medium. There are, therefore, some striking parallels between the open **channel** properties of the **stretch-activated** cation **channel** and the response of the whole lens or single lens cells to removal of extracellular Ca2+. There are also inconsistencies. This channel is apparently not open in the normal resting lens so removal of extracellular Ca2+ must cause it to open if it is indeed responsible for the increase in lens conductance. However, an increase in open probability at the single-channel level when external divalents are removed was not convincingly demonstrated.
IT **7440-54-2**, Gadolinium, biological studies
RL: BIOL (Biological study)
(eye lens conductance and **stretch-activated** cation **channel** response to)

L128 ANSWER 12 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2002324911 EMBASE
TITLE: Trabeculectomy and angle closure [3].
AUTHOR: Roberts T.; Francis I.; Lertusumitkul S.; Kappagoda M.; **Coroneo M.**
SOURCE: Ophthalmology, (2002) 109/9 (1584-1585).
Refs: 3
ISSN: 0161-6420 CODEN: OPHTDG
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 012 Ophthalmology
LANGUAGE: English

L128 ANSWER 13 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2002385191 EMBASE
TITLE: Acute angle closure glaucoma following the use of intranasal cocaine during dacryocystorhinostomy [1].
AUTHOR: Wilcsek G.A.; Vose M.J.; Francis I.C.; Sharma S.; **Coroneo M.T.**
CORPORATE SOURCE: Prof. M.T. Coroneo, Ocular Plastics Unit, Eye Clinic, Prince of Wales Hospital, High St, Randwick, NSW 2031,

Australia. m.coroneo@unsw.edu.au
SOURCE: British Journal of Ophthalmology, (1 Nov 2002) 86/11 (1312).
Refs: 8
ISSN: 0007-1161 CODEN: BJOPAL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L128 ANSWER 14 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2002269379 EMBASE
TITLE: Recognition and management of acute glaucoma.
AUTHOR: Attebo K.; **Coroneo M.**
CORPORATE SOURCE: Dr. K. Attebo, University of New South Wales, Prince of Wales Hospital, Glaucoma Unit, Sydney, NSW, Australia
SOURCE: Medicine Today, (2002) 3/7 (32-39).
ISSN: 1443-430X CODEN: MTNBCV
COUNTRY: Australia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
012 Ophthalmology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB .bul. Acute angle closure glaucoma is a medical emergency that requires immediate referral to an ophthalmologist. .bul. During a subacute glaucoma attack, patients may see rainbow-coloured haloes around lights and have some mistiness of vision and eye discomfort. These symptoms always warrant referral to an ophthalmologist. .bul. Acute glaucoma causes sudden profound reduction of vision, severe pain in and around the eye and often nausea and vomiting. Cardinal signs include a red eye, with a mid-dilated, fixed ovoid pupil and a cloudy cornea. .bul. The differential diagnoses are those of 'the acute red eye', which include iritis, conjunctivitis, keratitis and episcleritis. .bul. Acute glaucoma may be prevented by laser peripheral iridotomy.

L128 ANSWER 15 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2001123792 EMBASE
TITLE: Steroids and the eye.
AUTHOR: Watson S.; **Coroneo M.**
CORPORATE SOURCE: Dr. S. Watson, Department of Ophthalmology, The Prince of Wales Hospital, Randwick, NSW, Australia
SOURCE: Medicine Today, (2001) 2/3 (79-85).
ISSN: 1443-430X CODEN: MTNBCV
COUNTRY: Australia
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB .ovrhdot. The correct use of corticosteroids for ophthalmic conditions can be sight saving; their incorrect use is potentially blinding. .ovrhdot. Corticosteroids should never be given for an undiagnosed red eye, when visual acuity is impaired or if there is a history of ocular herpes infection. .ovrhdot. Corticosteroids should be prescribed only when indicated, not casually for the relief of ocular discomfort. .ovrhdot. Topical corticosteroid treatment should not be repeated or renewed without

regular review by an ophthalmologist. .ovrhdot. Patients on prolonged systemic corticosteroids should have six-monthly eye examinations by an ophthalmologist. .ovrhdot. Paediatric patients on corticosteroids require careful ophthalmological monitoring.

L128 ANSWER 16 OF 16 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-352677 [33] WPIDS
DOC. NO. CPI: C2003-092930
TITLE: Composition for protecting neural tissue from pressure induced apoptotic cell death caused by, e.g., **glaucoma**, comprises compound(s) which blocks the effects of pressure on neuronal cells.
DERWENT CLASS: B04
INVENTOR(S): **CORONEO, M T**
PATENT ASSIGNEE(S): (CORO-I) CORONEO M T
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002187919	A1	20021212	(200333)*		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002187919	A1 Cont of	US 2000-649643	20000829
		US 2002-84604	20020227

PRIORITY APPLN. INFO: US 2000-649643 20000829; US 2002-84604 20020227

AB US2002187919 A UPAB: 20030526
NOVELTY - Composition for protecting neural tissue from pressure induced apoptotic cell death comprises at least one compound which blocks the effects of pressure on neuronal cells, optionally in association with carrier(s) or excipient(s).
ACTIVITY - Ophthalmological.
MECHANISM OF ACTION - Pressure Effect Blocker; Stretch-activated Channel Blocker.
No biological data is given.
USE - The composition is used to protect neural tissue from pressure induced apoptotic cell death by administering a compound(s) which blocks the stretch activated channels (directly or indirectly) or other pressure sensitive cellular mechanisms on neuronal cells (eye or brain neuronal cells). It is used to treat **glaucoma**, elevated brain pressure, and peripheral nerve damage which cause neural cell apoptotic damage (all claimed).
ADVANTAGE - The invention makes use of compounds that can be readily identified by conventional physiological techniques. It can be formulated with standard buffers, excipients, and carriers.
Dwg.0/0

=>

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=> fil capl
FILE 'CAPLUS' ENTERED AT 16:49:47 ON 12 AUG 2003
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FILE COVERS 1907 - 12 Aug 2003  VOL 139 ISS 7
FILE LAST UPDATED: 11 Aug 2003  (20030811/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> d que l16; d que l22; d que l19

L6            1 SEA FILE=REGISTRY ABB=ON  GADOLINIUM/CN
L7        22915 SEA FILE=CAPLUS ABB=ON  L6
L9         4449 SEA FILE=CAPLUS ABB=ON  (GLAUCOMA OR ANTIGLAUCOMA)/OBI
L16           2 SEA FILE=CAPLUS ABB=ON  L7 AND L9



L6            1 SEA FILE=REGISTRY ABB=ON  GADOLINIUM/CN
L7        22915 SEA FILE=CAPLUS ABB=ON  L6
L10       56740 SEA FILE=CAPLUS ABB=ON  APOPTOSIS/OBI
L12       27178 SEA FILE=CAPLUS ABB=ON  PRESSURE/CT
L13       58165 SEA FILE=CAPLUS ABB=ON  EYE/CT
L14         468 SEA FILE=CAPLUS ABB=ON  STRETCH(W)(ACTIVAT? OR INDUC?)(3A)CHANN
                EL#
L21       26282 SEA FILE=CAPLUS ABB=ON  RETINA?/OBI
L22           3 SEA FILE=CAPLUS ABB=ON  L7 AND (L10 OR L12 OR L14) AND (L13 OR
                L21)



L6            1 SEA FILE=REGISTRY ABB=ON  GADOLINIUM/CN
L7        22915 SEA FILE=CAPLUS ABB=ON  L6
L11         634 SEA FILE=CAPLUS ABB=ON  ANTIAPOPTO?/OBI
L19           0 SEA FILE=CAPLUS ABB=ON  L11 AND L7


=> s (l16 or l22)  not l123

L129          3 (L16 OR L22)  NOT L123

=> fil medl;d que l41; d que l42

FILE 'MEDLINE' ENTERED AT 16:49:49 ON 12 AUG 2003

 FILE LAST UPDATED: 9 AUG 2003 (20030809/UP).  FILE COVERS 1958 TO DATE.
```

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L27	4252	SEA	FILE=MEDLINE ABB=ON	GADOLINIUM/CT
L31	25217	SEA	FILE=MEDLINE ABB=ON	OCULAR HYPERTENSION+NT/CT
L32	53979	SEA	FILE=MEDLINE ABB=ON	APOPTOSIS+NT/CT
L35	4518	SEA	FILE=MEDLINE ABB=ON	RETINAL GANGLION CELLS/CT
L38	17143	SEA	FILE=MEDLINE ABB=ON	INTRAOCULAR PRESSURE/CT
L41	1	SEA	FILE=MEDLINE ABB=ON	L27 AND (L31 OR (L32 AND L35) OR L38)

L27	4252	SEA	FILE=MEDLINE ABB=ON	GADOLINIUM/CT
L33	454	SEA	FILE=MEDLINE ABB=ON	STRETCH(W)(ACTIVAT? OR INDUC?)(3A)CHANNEL#
L34	66112	SEA	FILE=MEDLINE ABB=ON	ION CHANNELS+NT/CT
L36	1169	SEA	FILE=MEDLINE ABB=ON	L34(L)AI/CT
L40	245229	SEA	FILE=MEDLINE ABB=ON	NEURONS+NT/CT
L42	1	SEA	FILE=MEDLINE ABB=ON	L27 AND L33 AND L36 AND L40

=> s (l41 or l42) not l37

L130 2 (L41 OR L42) NOT L37

=> fil embase; d que l64; d que l65; d que l73

FILE 'EMBASE' ENTERED AT 16:49:50 ON 12 AUG 2003

FILE COVERS 1974 TO 10 Aug 2003 (20030810/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L53	4196	SEA	FILE=EMBASE ABB=ON	GADOLINIUM/CT
L54	22630	SEA	FILE=EMBASE ABB=ON	GLAUCOMA+NT/CT
L55	12278	SEA	FILE=EMBASE ABB=ON	INTRAOCULAR PRESSURE/CT
L56	4805	SEA	FILE=EMBASE ABB=ON	INTRAOCULAR PRESSURE ABNORMALITY+NT/CT
L62	344	SEA	FILE=EMBASE ABB=ON	GADOLINIUM CHLORIDE/CT
L64	4	SEA	FILE=EMBASE ABB=ON	(L53 OR L62) AND (L54 OR L55 OR L56)

L53	4196	SEA	FILE=EMBASE ABB=ON	GADOLINIUM/CT
L57	4217	SEA	FILE=EMBASE ABB=ON	RETINA GANGLION CELL/CT
L62	344	SEA	FILE=EMBASE ABB=ON	GADOLINIUM CHLORIDE/CT
L65	1	SEA	FILE=EMBASE ABB=ON	(L53 OR L62) AND L57

```
L53        4196 SEA FILE=EMBASE ABB=ON  GADOLINIUM/CT
L60         424 SEA FILE=EMBASE ABB=ON  STRETCH(W)(ACTIVAT? OR INDUC?)(3A)CHANN
                EL#
L61       21697 SEA FILE=EMBASE ABB=ON  CHANNEL BLOCKING
L62         344 SEA FILE=EMBASE ABB=ON  GADOLINIUM CHLORIDE/CT
L69      108856 SEA FILE=EMBASE ABB=ON  EYE+NT/CT OR RETINA+NT/CT
L72      182169 SEA FILE=EMBASE ABB=ON  NERVE CELL+NT/CT
L73           2 SEA FILE=EMBASE ABB=ON  L60 AND L61 AND (L53 OR L62) AND (L69
                OR L72)


=> s (l64 or l65 or l73) not l63

L131          7 (L64 OR L65 OR L73) NOT L63

=> fil wpids

FILE 'WPIDS' ENTERED AT 16:49:52 ON 12 AUG 2003
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FILE LAST UPDATED:          8 AUG 2003      <20030808/UP>
MOST RECENT DERWENT UPDATE:     200351        <200351/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

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    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

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    PLEASE VISIT:
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    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> d que l83; d que l87; d que l88; d que l89

L74        7836 SEA FILE=WPIDS ABB=ON  GADOLINIUM OR GD
L75        4534 SEA FILE=WPIDS ABB=ON  ?GLAUCOMA?
L83           8 SEA FILE=WPIDS ABB=ON  L74 AND L75



L74        7836 SEA FILE=WPIDS ABB=ON  GADOLINIUM OR GD
L78           6 SEA FILE=WPIDS ABB=ON  STRETCH(W)(ACTIVAT? OR INDUC?)(3A)CHANNE
                L#
L79           3 SEA FILE=WPIDS ABB=ON  L78(5A)(BLOCK? OR ANTAGONI? OR INHIBIT?)

L87           0 SEA FILE=WPIDS ABB=ON  L79 AND L74



L74        7836 SEA FILE=WPIDS ABB=ON  GADOLINIUM OR GD
L80        1406 SEA FILE=WPIDS ABB=ON  (INTRAOCULAR OR INTRA OCULAR)(3A)PRESSUR
                E#
L88           1 SEA FILE=WPIDS ABB=ON  L80 AND L74
```

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L74         7836 SEA FILE=WPIDS ABB=ON  GADOLINIUM OR GD
L76         4500 SEA FILE=WPIDS ABB=ON  RETINA?
L77         4056 SEA FILE=WPIDS ABB=ON  ?APOPTO?
L89            2 SEA FILE=WPIDS ABB=ON  L76 AND L77 AND L74


=> s (l83 or l88 or l89) not l82

L132          10 (L83 OR L88 OR L89) NOT L82

=> fil drugu; d que l102; d que l111

FILE 'DRUGU' ENTERED AT 16:49:55 ON 12 AUG 2003
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FILE LAST UPDATED: 7 AUG 2003       <20030807/UP>
>>>  DERWENT DRUG FILE (SUBSCRIBER)  <<<

>>>  SDI'S MAY BE RUN WEEKLY OR MONTHLY AS OF JUNE 2001.  <<<
>>>  (WEEKLY IS THE DEFAULT). FOR PRICING INFORMATION     <<<
>>>  SEE HELP COST                                        <<<

>>>  FILE COVERS 1983 TO DATE  <<<
>>>  THESAURUS AVAILABLE IN /CT  <<<



L90          159 SEA FILE=DRUGU ABB=ON  GADOLINIUM/CT
L92         1760 SEA FILE=DRUGU ABB=ON  GLAUCOMA? OR ANTIGLAUCOMA?
L93         3764 SEA FILE=DRUGU ABB=ON  RETINA?
L94        16775 SEA FILE=DRUGU ABB=ON  APOPTO? OR ANTIAPOPTO?
L95         1554 SEA FILE=DRUGU ABB=ON  (INTRAOCULAR OR INTRA OCULAR)(3A)PRESSUR
                 E#
L102           1 SEA FILE=DRUGU ABB=ON  L90 AND (L92 OR L93 OR L94 OR L95)



L90          159 SEA FILE=DRUGU ABB=ON  GADOLINIUM/CT
L96           28 SEA FILE=DRUGU ABB=ON  STRETCH(W)(ACTIVAT? OR INDUC?)(3A)CHANNE
                 L#
L103        5662 SEA FILE=DRUGU ABB=ON  NEURON/CT
L107           5 SEA FILE=DRUGU ABB=ON  STRETCH/CT AND ACTIVATED/CT AND
                 CHANNEL/CT
L109        6232 SEA FILE=DRUGU ABB=ON  EYE/CT OR EYE -DISEASE/CT
L110       12535 SEA FILE=DRUGU ABB=ON  EYE-DISEASE/CT
L111           0 SEA FILE=DRUGU ABB=ON  L90 AND (L96 OR L107) AND (L103 OR
                 (L109 OR L110))

=> fil biosis; d que l122

FILE 'BIOSIS' ENTERED AT 16:49:56 ON 12 AUG 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 6 August 2003 (20030806/ED)


L113       10064 SEA FILE=BIOSIS ABB=ON  GADOLINIUM OR GD
```

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L114       22206 SEA FILE=BIOSIS ABB=ON  ?GLAUCOMA?
L115       12858 SEA FILE=BIOSIS ABB=ON  (INTRAOCULAR OR INTRA OCULAR)(3A)PRESSU
                 RE#
L122           9 SEA FILE=BIOSIS ABB=ON  L113 AND (L114 OR L115)


=> dup rem l130,l102,l129,l122,l131,l132
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FILE 'DRUGU' ENTERED AT 16:50:39 ON 12 AUG 2003
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PROCESSING COMPLETED FOR L130
PROCESSING COMPLETED FOR L102
PROCESSING COMPLETED FOR L129
PROCESSING COMPLETED FOR L122
PROCESSING COMPLETED FOR L131
PROCESSING COMPLETED FOR L132
L133          29 DUP REM L130 L102 L129 L122 L131 L132 (3 DUPLICATES REMOVED)
                 ANSWERS '1-2' FROM FILE MEDLINE
                 ANSWER '3' FROM FILE DRUGU
                 ANSWERS '4-6' FROM FILE CAPLUS
                 ANSWERS '7-15' FROM FILE BIOSIS
                 ANSWERS '16-21' FROM FILE EMBASE
                 ANSWERS '22-29' FROM FILE WPIDS

=> d ibib ab hitrn 1-29; fil hom

L133 ANSWER 1 OF 29     MEDLINE on STN
ACCESSION NUMBER:    1999315368      MEDLINE
DOCUMENT NUMBER:     99315368   PubMed ID: 10383616
TITLE:               Stretch-activated cation
                     channels of leech neurons: characterization and
                     role in neurite outgrowth.
AUTHOR:              Calabrese B; Manzi S; Pellegrini M; Pellegrino M
CORPORATE SOURCE:    Dipartimento di Fisiologia e Biochimica 'G. Moruzzi',
                     Universita di Pisa, Via S. Zeno 31, 56127, Italy.
SOURCE:              EUROPEAN JOURNAL OF NEUROSCIENCE, (1999 Jul) 11 (7)
                     2275-84.
                     Journal code: 8918110. ISSN: 0953-816X.
PUB. COUNTRY:        France
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals; Space Life Sciences
ENTRY MONTH:         199907
ENTRY DATE:          Entered STN: 19990816
                     Last Updated on STN: 19990816
                     Entered Medline: 19990730
AB   The goal of this study was to characterize the stretch-
     activated ion channels (SACs) of adult identified
```

neurons of the leech Hirudo medicinalis and to test the role of SACs in neurite outgrowth of isolated cells. Using cell-attached patch recording, we established that SACs are densely distributed in the growth cone membrane of cultured neurons. In excised patches, we found that these channels are permeable to Ca2+, as well as to monovalent cations. The channels are blocked by the extracellular application of gadolinium (Gd3+), amiloride and gentamicin. Amiloride and gentamicin, respectively, induce a partial and complete voltage-dependent block. Time-lapse video recordings of neurite outgrowth from single cultured neurons were used to study the effects of blocking SACs with gentamicin. Within 20 h of plating in the presence of the aminoglycoside, the total length of neuronal arborization was significantly greater than that measured in its absence. The amount of assembled axon per unitary surface area remained constant over 40 h and did not differ significantly with or without gentamicin. Our findings show that SACs of leech neurons admit Ca2+, are densely distributed in the growth cone membrane and exhibit typical pharmacological features of mechanotransducer ion channels. In addition, our data suggest that these cation channels participate in the early interaction between growing neurites and culture substrate.

L133 ANSWER 2 OF 29 MEDLINE on STN
ACCESSION NUMBER: 93356678 MEDLINE
DOCUMENT NUMBER: 93356678 PubMed ID: 8352692
TITLE: Strabismus following implantation of Baerveldt drainage devices.
AUTHOR: Munoz M; Parrish R K 2nd
CORPORATE SOURCE: Bascom Palmer Eye Institute, Miami, Fla.
SOURCE: ARCHIVES OF OPHTHALMOLOGY, (1993 Aug) 111 (8) 1096-9. Journal code: 7706534. ISSN: 0003-9950.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19931001
Last Updated on STN: 19980206
Entered Medline: 19930913

AB OBJECTIVE: To describe the clinical features of strabismus following implantation of a Baerveldt glaucoma seton. DESIGN: Case series of four patients with a minimum follow-up of 6 months. SETTING: Specialized glaucoma referral center at Bascom Palmer Eye Institute/Ann Bates Leach Eye Hospital, Miami, Fla. PATIENTS: Consecutive sample of four patients with persistent binocular diplopia following implantation of a 350-mm2 Baerveldt glaucoma seton in the superotemporal quadrant. RESULTS: Each patient presented with a characteristic pattern of either exotropia or hypertropia, or both. The deviation increased with gaze opposite the ipsilateral superior and lateral muscles and decreased in the field of action of the involved muscles. All patients demonstrated a convergence insufficiency type of exotropia. CONCLUSION: These patients presented with a similar type of restrictive strabismus. Proposed mechanisms include an increase in the length-tension curve of the muscle induced by the underlying bleb and a posterior fixation effect as a result of scarring behind the implant.

L133 ANSWER 3 OF 29 DRUGU COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-45680 DRUGU P B
TITLE: Motexafin gadolinium increases **apoptotic** response to radiation in vitro and in vivo.
AUTHOR: Woodburn K; Luo Y; Qing F; Voehringer D W; Miller R A
CORPORATE SOURCE: Pharmacyclics; Stanford-Med.Sch.
LOCATION: Sunnyvale; Stanford, Cal., USA
SOURCE: Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 90, 2001) ISSN : 0197-016X

AVAIL. OF DOC.: Pharmacyclics, Sunnyvale, California, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The in-vitro intracellular localization of motexafin gadolinium (gadolinium texaphyrin, Xcytrin) in **apoptotic**-sensitive (LYas) and -resistant (Lyar) murine lymphoma cell lines and its ability to enhance the **apoptotic** response to radiation in mice was investigated. Xcytrin was localized to the extranuclear compartment of the tumor cells, in-vitro, and in-vitro and in-vivo enhanced the tumor response to radiation. Results suggest that Xcytrin increases the **apoptotic** response to radiation. (conference abstract: 92nd Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, USA, 2001).

L133 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2001:452877 CAPLUS
DOCUMENT NUMBER: 135:81966
TITLE: Phosphoglycerate kinase in the treatment of disease
INVENTOR(S): Lay, Angelina J.; Hogg, Philip John
PATENT ASSIGNEE(S): Unisearch Limited, Australia
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043767	A1	20010621	WO 2000-AU1542	20001213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1244467	A1	20021002	EP 2000-984641	20001213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: AU 1999-4754 A 19991217
WO 2000-AU1542 W 20001213

AB The present invention provides a pharmaceutical compn. for the inhibition of angiogenesis assocd. with disease in a vertebrate, said compn. comprising phosphoglycerate kinase, or a fragment(s) or analog thereof, together with a pharmaceutically acceptable carrier, adjuvant and/or diluent. The present invention also relates to the treatment of disease, esp. cancer, in a vertebrate via the administration of a therapeutically effective amt. of phosphoglycerate kinase (PGK), or fragment(s) or analog thereof.
IT **7440-54-2D**, Gadolinium, chelates, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(phosphoglycerate kinase for antitumor inhibition of angiogenesis)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2000:493550 CAPLUS

DOCUMENT NUMBER: 133:101736
TITLE: A reagent system and method for increasing the luminescence of lanthanide(iii) macrocyclic complexes
INVENTOR(S): Leif, Robert C.; Vallarino, Lidia
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042048	A1	20000720	WO 2000-US1211	20000118
W: CA, CH, DE, FI, GB, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2360054	AA	20000720	CA 2000-2360054	20000118
EP 1150985	A1	20011107	EP 2000-905653	20000118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6340744	B1	20020122	US 2000-484670	20000118
US 2002132992	A1	20020919	US 2001-10597	20011206

PRIORITY APPLN. INFO.: US 1999-116316P P 19990119
US 2000-484670 A1 20000118
WO 2000-US1211 W 20000118
OTHER SOURCE(S): MARPAT 133:101736

AB Disclosed are a spectrofluorimetrically detectable luminescent compn. and processes for enhancing the luminescence of one or more lanthanide-contg. macrocycles. The luminescent compn. comprises a micelle-producing amt. of at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compd. having an emission spectrum peak in the range from 500 to 950 nm, and a luminescence-enhancing amt. of at least one energy transfer donor compd. of yttrium or a 3-valent lanthanide element having at. no. 59-71, provided that the lanthanide element of said macrocycle compd. and the lanthanide element of said energy transfer donor compd. are not identical. The addn. of gadolinium(III) in the presence of other solutes to both the prototype and the difunctionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patents #5,373,093 and #5,696,240, enhances their luminescence. Similar enhancements of luminescence also results for the mono-functionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patent #5,696,240. The enhanced luminescence afforded by the compn. enables the detection and/or quantitation of many analytes in low concns. without the use of expensive, complicated time-gated detection systems.

IT **7440-54-2**, Gadolinium, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (reagent system and method for increasing luminescence of lanthanide(iii) macrocyclic complexes)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L133 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:588649 CAPLUS
DOCUMENT NUMBER: 117:188649
TITLE: Divalent cation effects on lens conductance and **stretch-activated** cation **channels**
AUTHOR(S): Rae, James L.; Mathias, Richard T.; Cooper, Kim; Baldo, George
CORPORATE SOURCE: Dep. Physiol., Mayo Found., Rochester, MN, 55905, USA

Searched by Barb O'Bryen, STIC 308-4291

SOURCE: Experimental Eye Research (1992), 55(1), 135-44
CODEN: EXERA6; ISSN: 0014-4835
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In patch clamp studies of apical membrane from frog lens epithelium, the most frequently obsd. **channel** is **stretch-activated,** highly selective for cations over anions but showing little selectivity for Na+ vs. K+. In normal physiol. saline, the open channel conductance is 25-30 pS and quite linear over .+-. 100 mV. In the absence of extracellular divalent ions, the open channel conductance for inward current flow increases to about 50 pS at the normal lens resting voltage of -75 mV, whereas the conductance for outward current flow is unaffected. In the intact lens, removal of extracellular divalents causes the input conductance approx. to double and the intracellular voltage to depolarize from -74 to -58 mV. A variety of divalent ions block this change in whole lens conductance and voltage in the same order in which they block the stretch channels. Single voltage-clamped epithelial cells also increase their conductance when Ca2+ is removed from their bathing medium. There are, therefore, some striking parallels between the open **channel** properties of the **stretch-activated** cation **channel** and the response of the whole lens or single lens cells to removal of extracellular Ca2+. There are also inconsistencies. This channel is apparently not open in the normal resting lens so removal of extracellular Ca2+ must cause it to open if it is indeed responsible for the increase in lens conductance. However, an increase in open probability at the single-channel level when external divalents are removed was not convincingly demonstrated.

IT **7440-54-2**, Gadolinium, biological studies
RL: BIOL (Biological study)
(eye lens conductance and **stretch-activated** cation **channel** response to)

L133 ANSWER 7 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
ACCESSION NUMBER: 2003:279462 BIOSIS
DOCUMENT NUMBER: PREV200300279462
TITLE: Left-sided facial nevus with contralateral leptomeningeal angiomatosis in a child with Sturge-Weber syndrome: Case report.
AUTHOR(S): Widdess-Walsh, Peter; Friedman, Neil Roy (1)
CORPORATE SOURCE: (1) Department of Neurology, Cleveland Clinic Foundation, 9500 Euclid Avenue, S71, Cleveland, OH, 44195, USA: friedmn@ccf.org USA
SOURCE: Journal of Child Neurology, (April 2003, 2003) Vol. 18, No. 4, pp. 304-305. print.
ISSN: 0883-0738.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Sturge-Weber syndrome is characterized by a facial vascular nevus associated with an ipsilateral leptomeningeal angioma. Variants of this classical presentation have been described in the literature, some of which have prognostic significance. We report a magnetic resonance imaging (MRI)-confirmed variant of a leptomeningeal angioma contralateral to the facial nevus. We describe one patient with Sturge-Weber syndrome who presented with a left-sided facial nevus, left eye **glaucoma**, episodes of left-sided weakness, and right-sided leptomeningeal angiomatosis by **gadolinium**-enhanced brain MRI. The literature regarding variants of Sturge-Weber syndrome and their prognosis is reviewed. The prognosis for this variant is likely similar to Sturge-Weber syndrome with an ipsilateral leptomeningeal angioma.

L133 ANSWER 8 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:121825 BIOSIS

DOCUMENT NUMBER: PREV200300121825
TITLE: Detection of **glaucomatous** visual field defect by nonconventional perimetry.
AUTHOR(S): Iester, Michele (1); Altieri, Michele; Vittone, Paolo; Calabria, Giovanni; Zingirian, Mario; Traverso, Carlo E.
CORPORATE SOURCE: (1) Viale Teano 71/1, 16147, Genoa, Italy: m_iester@hotmail.com Italy
SOURCE: American Journal of Ophthalmology, (January 2003, 2003) Vol. 135, No. 1, pp. 35-39. print. ISSN: 0002-9394.
DOCUMENT TYPE: Article
LANGUAGE: English
AB PURPOSE: To report the correlations among Humphrey Field Analyzer 750 (HFA), high-pass resolution perimetry (HRP), and frequency-doubling technology (FDT) perimetry in **glaucoma** patients and ocular hypertensive patients, DESIGN: Cross-sectional study, METHODS: Eighty-two eyes of 82 consecutive patients with primary open-angle **glaucoma** (POAG) or ocular hypertension were included in this study. One eye of each patient was randomly selected for data analysis. Visual fields were assessed by HFA, HRP, and FDT perimetry. HRP global deviation (HRP-**GD**), HRP local deviation (HRP-LD), FDT-mean deviation (FDT-MD), and FDT-pattern standard deviation (FDT-PSD) were considered for the analysis. Clinical agreement between HRP and FDT was evaluated. All data were analyzed by Pearson r coefficient when the distribution of the data was normal and by Spearman coefficient correlation when the distribution of the data was not normal. A P<.05 was considered statistically significant, RESULTS: Fifty-two eyes (52 patients) were classified as **glaucoma** and 30 eyes (30 patients) as ocular hypertension. In the entire group, a significant (P>.001) correlation was found between the HFA indices and those of either HRP or FDT. A significant (P<.001) correlation was found between HRP-**GD** and FDT-MD as well as between HRP-LD and FDT-PSD. In 14% of the **glaucomatous** patients and in 33% of the subjects with ocular hypertension, FDT and HRP showed different clinical features, CONCLUSIONS: Our data suggest that FDT and HRP are useful for detection of early **glaucomatous** visual field damage.

L133 ANSWER 9 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:54888 BIOSIS
DOCUMENT NUMBER: PREV200300054888
TITLE: A case of granular cell tumor of the orbit.
AUTHOR(S): Kawana, Keisuke (1); Nose, Harumi; Honmura, Sachiko
CORPORATE SOURCE: (1) Department of Ophthalmology, Tsukuba University Hospital, 2-1-1 Amakubo Tsukuba-shi, Ibaragi-ken, 305-8576, Japan Japan
SOURCE: Rinsho Ganka, (2002) Vol. 56, No. 10, pp. 1497-1501. print. ISSN: 0370-5579.
DOCUMENT TYPE: Article
LANGUAGE: Japanese
AB A 52-year-old male presented with vertical diplopia. He had noticed a hard mass in the lower margin of the orbit 2 months before. He showed no abnormal findings except the orbital tumor and **intraocular pressure** of 24 mmHg in his right eye. Computerized tomography (CT) and magenetic resonance imaging (MRI) showed a tumor inferior to the right eyeball. Calcification or bone destruction was absent. MRI imaging of the tumor showed intermediate intensity on T1-weighted image and low intensity on T2-weighted image. The tumor showed slight enhancement with **gadolinium**-DTPA. Surgery showed a hard tumor mass measuring 20 mm X 12 mm X 12 mm in size. By histopathology, the tumor cells had abundant cytoplasm and eosino- philic granules. The tumor was diagnosed with granular cell tumor, which is a rare occurrence in the orbit, after immuohistologic studies showed positive for S-100 protein.

L133 ANSWER 10 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:95880 BIOSIS
DOCUMENT NUMBER: PREV200100095880
TITLE: Correlation between high-pass resolution perimetry and standard threshold perimetry in subjects with **glaucoma** and ocular hypertension.
AUTHOR(S): Iester, Michele (1); Capris, Paolo; Altieri, Michele; Zingirian, Mario; Traverso, Carlo E.
CORPORATE SOURCE: (1) Department of Neurological and Visual Sciences, Ophthalmology B, University of Genoa, c/o v.le Teano 71/1, 16147, Genoa: iester@csita.unige.it Italy
SOURCE: International Ophthalmology, (1999) Vol. 23, No. 2, pp. 99-103. print.
ISSN: 0165-5701.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose: To evaluate the correlation between High-Pass Resolution Perimetry (HRP) and standard threshold perimetry in patients with **glaucoma** or ocular hypertension. Methods: 31 **glaucomatous** patients and 37 ocular hypertension subjects with previous perimetric examination experience were consecutively recruited and only one eye for each patient was selected at random. **Glaucomatous** patients were classified as having primary open angle **glaucoma** when they had an abnormal visual field and/or an abnormal optic nerve head (ONH)/retinal nerve fiber layer (RNFL) typical of **glaucoma**, open angle at gonioscopy and no clinically apparent secondary cause for their **glaucoma**. Ocular hypertension subjects were defined as having **intraocular pressure** >21 mm Hg on no treatment, normal visual field, normal ONH and RNFL, elevated **intraocular pressure** without any treatment. All the subjects were examined with Humphrey Field Analyzer (HFA) 640, 'program central 30-2' (Humphrey Systems, San Leandro, CA, USA) and with High-Pass Resolution Perimeter (HRP), Ophthimus version 2.4, 'ring program' (Nikon-HighTech Vision, Goteborg, Sweden). Visual field indices were obtained with both systems: for HFA mean deviation (MD), corrected pattern standard deviation (CPSD) and short term fluctuation (SF), while for HRP global deviation (**GD**), local deviation (LD), form index (FI) and neural capacity (NC). The data were analyzed by descriptive analysis, Student's t test with Bonferroni's correction or Mann-Whitney non-parametric test and Pearson or Spearman's correlation coefficient. Results: A significant correlation was found between MD and **GD** ($r = -0.81$), CPSD and LD ($r = 0.87$), PSD and LD ($r = 0.72$). NC was significantly correlated with MD ($r = 0.76$), **GD** ($r = -0.94$). FI was significantly correlated with PSD ($r = -0.58$), CPSD ($r = -0.72$), LD ($r = -0.56$). When the same data were analyzed for the **glaucomatous** group only, similar results were found; in the ocular hypertensive group no significant correlation was found except between NC and MD ($r = 0.52$). Conclusion: HRP indices vary comparably with HFA indices. Parameters as NC and FI were significantly correlated with standard visual field indices of both HFA and HRP. Although the clinical applications for FI are not clear yet, NC could detect both early **glaucomatous** damage and age related changes.

L133 ANSWER 11 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:41757 BIOSIS
DOCUMENT NUMBER: PREV199698613892
TITLE: Magnetic resonance imaging in the early diagnosis of cavernous sinus thrombosis.
AUTHOR(S): Igarashi, Hiromasa (1); Igarashi, Sachiko; Fujio, Naoki; Fukui, Katsuhiko; Yoshida, Akitoshi
CORPORATE SOURCE: (1) Dep. Ophthalmol., Asahikawa Med. Coll., 4-5 Nishikagura, Asahikawa 078 Japan
SOURCE: Ophthalmologica, (1995) Vol. 209, No. 5, pp. 292-296.
ISSN: 0030-3755.

DOCUMENT TYPE: Article
LANGUAGE: English
AB A 55-year-old man reported a severe headache of 3 days' duration, left ptosis and left lid swelling before examination. The ocular examination revealed left eye proptosis, severe edema of the left bulbar conjunctiva and lid; increasing **intraocular pressure** of the left eye and ptosis on the left side with decreased extraocular movement. The right eye was normal. Hematologic studies indicated mild inflammation. An enhanced computed tomography scan revealed proptosis of the left globe and enlargement of the superior ophthalmic vein and cavernous sinus of the left-side. Angiography revealed an area of interrupted blood flow in the left cavernous sinus. Enhanced magnetic resonance imaging (MRI) with **Gd**-DTPA revealed a low-intensity area that was suspected to be a blood clot in the enlarged left cavernous sinus. This case indicates the efficacy of enhanced MRI examination in the early diagnosis of cavernous sinus thrombosis.

L133 ANSWER 12 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:65217 BIOSIS
DOCUMENT NUMBER: PREV199344030867
TITLE: Magnetic resonance imaging of the aqueous/water flow.
AUTHOR(S): Cheng, Hong-Ming
CORPORATE SOURCE: Howe Lab. Ophthalmol., Harvard Med. Sch., 243 Charles St., Boston, Mass. 02114
SOURCE: Experimental Eye Research, (1992) Vol. 55, No. SUPPL. 1, pp. S214.
Meeting Info.: X International Congress of Eye Research Stresa, Italy September 20, 1992
ISSN: 0014-4835.
DOCUMENT TYPE: Conference
LANGUAGE: English

L133 ANSWER 13 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:140862 BIOSIS
DOCUMENT NUMBER: BA91:77402
TITLE: **GADOLINIUM** DTPA-ENHANCED MAGNETIC RESONANCE IMAGING OF THE AQUEOUS FLOW IN THE RABBIT EYE.
AUTHOR(S): CHENG H-M; KWONG K K; XIONG J; CHANG C
CORPORATE SOURCE: HOWE LAB. OPHTHALMOL., HARVARD MED. SCH., BOSTON, MASS. 02114.
SOURCE: MAGN RESON MED, (1991) 17 (7), 237-243.
CODEN: MRMEEN. ISSN: 0740-3194.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Magnetic resonance imaging with **gadolinium**-diethylenetriaminepentaacetic acid complex (GdDTPA) as the contrast agent was used to image the aqueous chamber of the eye. This method, in addition to providing spatial information, permits quantitative study of the aqueous flow. GdDTPA solution was applied either topically or intravenously, entering the anterior chamber via different pathways. The wash-in and wash-out of GdDTPA follow a two-compartment model which enables determination of the aqueous flow rate by multiplying the aqueous chamber volume by the wash-out rate constant. Rabbit eyes showed a flow rate of 1.5-2 .mu.l/min which was retarded by the systemic administration of acetazolamide (Diamox).

L133 ANSWER 14 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1990:462646 BIOSIS
DOCUMENT NUMBER: BR39:98007
TITLE: MAGNETIC RESONANCE IMAGING OF THE AQUEOUS FLOW IN THE RABBIT EYE.
AUTHOR(S): CHENG H-M; KWONG K K; XIONG J; CHANG C
CORPORATE SOURCE: HOWE LAB. OPHTHALMOL., HARV. MED. SCH., BOSTON, MASS.

02114.
SOURCE: ANNUAL SPRING MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY, SARASOTA, FLORIDA, USA, APRIL 29-MAY 4, 1990. INVEST OPHTHALMOL VISUAL SCI, (1990) 31 (4 ABSTR ISSUE), 377.
CODEN: IOVSDA. ISSN: 0146-0404.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L133 ANSWER 15 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1985:384269 BIOSIS
DOCUMENT NUMBER: BA80:54261
TITLE: EVIDENCE OF EXTRAOCULAR MUSCLE RESTRICTION IN AUTOIMMUNE THYROID DISEASE.
AUTHOR(S): GAMBLIN G T; GALENTINE P; CHERNOW B; SMALLRIDGE R C; EIL C
CORPORATE SOURCE: ENDOCRINE BRANCH, NAVAL HOSP., PORTSMOUTH, VA. 23708.
SOURCE: J CLIN ENDOCRINOL METAB, (1985) 61 (1), 167-171.
CODEN: JCEMAZ. ISSN: 0021-972X.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Patients with Graves' disease lacking eye symptoms frequently have abnormal **intraocular pressure** (IOP) increases on upward gaze (.gtoreq. 3 mm Hg) indicative of apparent subclinical ophthalmopathy. Because of the close relationship between Graves' disease (**GD**) and Hashimoto's thyroiditis (HT), 30 patients with a history of HT as well as 26 patients with a history of **GD**, 4 patients with a history of subacute thyroiditis, 1 patient with a history of silent thyroiditis, and 25 normal subjects for the presence of IOP abnormalities at 15.degree. and 25.degree. upgaze were examined. While all of the patients were asymptomatic, had no exophthalmos and were euthyroid at the time of the exam, Hertel exophthalmometer readings (mean .+-. SD) for the patients with **GD** were significantly higher ($P < 0.005$) than those for either the HT patients or normal subjects (17.1 .+-. 2.4 vs. 14.5 .+-. 2.3 vs. 14.4 .+-. 4.2 mm, respectively). At 15.degree. upgaze, IOP abnormalities occurred in 25% and 13% of patients with **GD** and HT, respectively. AT 25.degree. upgaze, these figures rose to 54% for the **GD** patients and 37% in HT patients. Only 1 of 25 normal subjects had elevated IOP changes on upgaze, as did the 1 patient with silent thyroiditis, but the patients with subacute thyroiditis did not. The frequent presence of extraocular muscle restriction in patients with a history of HT as well as in patients with a history of **GD** was suggested. Maximal detection of these IOP abnormalities requires that patients be examined at 25.degree. upgaze. Apparently, the autoimmune bases of both **GD** and HT are closely linked, at least as manifested by eye muscle involvement.

L133 ANSWER 16 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2000417819 EMBASE
TITLE: [Sturge-Weber syndrome. The current neuro-imaging data]. SYNDROME DE STURGE-WEBER. DONNEES ACTUELLES DE L'IMAGERIE NEURORADIOLOGIQUE.
AUTHOR: Boukobza M.; Enjolras O.; Cambra M.R.; Merland J.J.
SOURCE: Journal de Radiologie, (2000) 81/7 (765-771).
Refs: 39
ISSN: 0221-0363 CODEN: JRMDAH
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
014 Radiology
021 Developmental Biology and Teratology
LANGUAGE: French
SUMMARY LANGUAGE: English; French

AB Sturge-Weber syndrome (SWS) is a rare congenital sporadic disease with neuro-ocular and cutaneous vascular findings. Clinically, the full-blown condition consists of a facial port-wine stain (PWS) involving the V1 facial trigeminal skin area, alone or in combination with V2 and V3 PWS, seizures and ocular abnormalities (glaucoma and choroidal angioma). Radiologically, a leptomeningeal (pial) capillary and venous malformation, mostly located in the parieto-occipital area, cerebral atrophy and calcifications are demonstrated. An ipsilateral enlarged choroid plexus may be an early anatomic symptom. Developmental venous anomalies (DVA) of the brain are sometimes associated. MR with gadolinium enhancement is the optimal neuro-diagnostic imaging technique for the screening of infants with an at-risk V1 PWS, as well as for the follow-up of patients with evidence SWS. Accelerated myelination in the involved hemisphere may be an early diagnostic feature before 6 months of age. Later, hyperintensity of white matter on T2 is considered a symptom of gliosis. Clinically, progression of the diseases is associated with anatomic changes and correlates with the extent of the pial vascular anomaly, extent and severity of cerebral atrophy, and white matter abnormalities. A neonatal neuro-imaging work-up, using CT or MRI, may not demonstrate the pial anomaly and should be repeated after 6 to 12 months in an at-risk infant with V1 PWS.

L133 ANSWER 17 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2000164232 EMBASE
TITLE: Identification of a peptide toxin from Grammostola spatulata spider venom that blocks cation-selective **stretch-activated channels**.
AUTHOR: Suchyna T.M.; Johnson J.H.; Hamer K.; Leykam J.F.; Gage D.A.; Clemo H.F.; Baumgarten C.M.; Sachs F.
CORPORATE SOURCE: T.M. Suchyna, Dept. of Physiology and Biophysics, 320 Cary Hall, SUNY, Buffalo, NY 14214, United States. suchyna@acsu.buffalo.edu
SOURCE: Journal of General Physiology, (2000) 115/5 (583-598). Refs: 58
ISSN: 0022-1295 CODEN: JGPLAD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have identified a 35 amino acid peptide toxin of the inhibitor cysteine knot family that blocks cab ionic **stretch-activated** ion **channels**. The toxin, denoted GsMTx-4, was isolated from the venom of the spider Grammostola spatulata and has <50% homology to other neuroactive peptides. It was isolated by fractionating whole venom using reverse phase HPLC, and then assaying fractions on **stretch-activated channels** (SACs) in outside-out patches from adult rat astrocytes. Although the channel gating kinetics were different between cell-attached and outside-out patches, the properties associated with the channel pore, such as selectivity, for alkali cations, conductance (.apprx.45 pS at -100 mV) and a mild rectification were unaffected by outside-out formation. GsMTx-4 produced a complete block of SACs in outside- out patches and appeared specific since it had no effect on whole-cell voltage-sensitive currents. The equilibrium dissociation constant of .apprx.630 nM was calculated from the ratio of association and dissociation rate constants. In hypotonically swollen astrocytes, GsMTx-4 produces .apprx.40% reduction in swelling-activated whole-cell current. Similarly, in isolated ventricular cells from a rabbit dilated cardiomyopathy model, GsMTx-4 produced a near complete block of the volume-sensitive cation-selective current, but did not affect the anion current. In the myopathic heart cells, where the swell- induced current is

tonically active, GsMTx-4 also reduced the cell size. This is the first report of a peptide toxin that specifically blocks stretch- activated currents. The toxin affect on swelling-activated whole-cell currents implicates SACs in volume regulation.

L133 ANSWER 18 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2000073488 EMBASE
TITLE: Cerebral blood flow and glucose metabolism in an infant with Sturge- Weber syndrome.
AUTHOR: Yu S.-M.; Chang C.-P.; Liao S.-Q.; Luo C.-B.; Sheu M.-H.; Liu R.-S.
CORPORATE SOURCE: Dr. R.-S. Liu, Department of Nuclear Medicine, Taipei Veterans General Hospital, No. 201, Sec. 2, Shih-Pai Road, Taipei, Taiwan, Province of China
SOURCE: Clinical Nuclear Medicine, (2000) 25/3 (217-218).
Refs: 3
ISSN: 0363-9762 CODEN: CNMEDK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
023 Nuclear Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A 15-month-old girl had Sturge-Weber syndrome associated with glaucoma in the left eye. No seizure or hemiparesis was present. Leptomeningeal angiomatosis was clearly shown by contrast-enhanced MRI and MR angiography. Positron emission tomography (PET) with O-15 water and F-18 fluorodeoxyglucose (FDG) was used to study blood flow and glucose metabolism in the brain. The O-15 water PET and FDG PET showed that the cerebral blood flow and glucose metabolism were dissimilar in the region of the leptomeningeal angiomatosis and the ipsilateral remote cerebral cortex.

L133 ANSWER 19 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 1998001061 EMBASE
TITLE: Guidance of CNS growth cones by substratum grooves and ridges: Effects of inhibitors of the cytoskeleton, calcium channels and signal transduction pathways.
AUTHOR: Rajnicek A.M.; McCaig C.D.
CORPORATE SOURCE: A.M. Rajnicek, Department of Biomedical Sciences, Institute of Medical Sciences, University of Aberdeen, Aberdeen AB25 2ZD, United Kingdom. a.m.rajnicek@abdn.ac.uk
SOURCE: Journal of Cell Science, (1997) 110/23 (2915-2924).
Refs: 61
ISSN: 0021-9533 CODEN: JNCSAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We exploited our observation that embryonic Xenopus spinal neurites align parallel to grooves in a quartz surface and that embryonic rat hippocampal neurites align perpendicular to shallow, narrow grooves to investigate the mechanism of growth cone contact guidance. Substratum topography affected the pattern of growth cone filopodia and microtubules but parallel orientation of Xenopus neurites and perpendicular orientation of hippocampal neurites were unperturbed by cytochalasin B, which virtually eliminated filopodia. Hippocampal growth cone orientation and turning in response to grooves was unaffected by disruption of microtubules using taxol or nocodazole. Gross cytoskeletal reorganization on grooved substrata was therefore not required for growth cone steering. Inhibitors were used to identify the signal transduction pathway for perpendicular

alignment of hippocampal neurites. Alignment persisted in the presence of gadolinium chloride, a blocker of **stretch-activated** calcium **channels**, the G protein inhibitor pertussis toxin, the protein tyrosine kinase inhibitor genistein, the protein kinase A and G inhibitor HA1004, the protein kinase A inhibitor KT5720 and the protein kinase G inhibitor KT5823. Low concentrations of the protein kinase C inhibitors staurosporine, bisindolylmaleimide or H-7 did not affect perpendicular orientation but higher concentrations inhibited it. The calcium channel blockers flunarizine, nifedipine and diltiazem also inhibited perpendicular orientation. Influx of calcium and protein kinase C activity therefore appear to be involved in perpendicular contact guidance.

L133 ANSWER 20 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 94341820 EMBASE
DOCUMENT NUMBER: 1994341820
TITLE: Choroidal infarction after optic nerve sheath fenestration.
AUTHOR: Rizzo III J.F.; Lessell S.
CORPORATE SOURCE: Massachusetts Eye and Ear Infirmary, 243 Charles St,Boston, MA 02114, United States
SOURCE: Ophthalmology, (1994) 101/9 (1622-1626).
ISSN: 0161-6420 CODEN: OPHTDG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Purpose: To describe a visual complication of optic nerve sheath fenestration. Methods: Case review of two patients who underwent seemingly uncomplicated optic nerve sheath fenestration. Findings: Both patients had a surgical complication that resulted in significant depression of their temporal visual field and development of a wedge-shaped region of subretinal pigmentation in the nasal fundus. Conclusions: Both patients had choroidal infarctions as a complication of optic nerve sheath fenestration. Choroidal infarction should be considered in cases of unexpected loss of visual field after this type of surgery, although the funduscopic signs that assist in making the diagnosis may not be evident for several weeks after surgery.

L133 ANSWER 21 OF 29 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 94380940 EMBASE
DOCUMENT NUMBER: 1994380940
TITLE: Part two: Annual review in neuro-ophthalmology: The anterior visual pathways.
AUTHOR: Sadun A.A.; Dao J.
CORPORATE SOURCE: Estelle Doheny Eye Institute, 1450 San Pablo Street,Los Angeles, CA 90033, United States
SOURCE: Journal of Neuro-Ophthalmology, (1994) 14/4 (234-249).
ISSN: 1070-8022 CODEN: JNEOEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
012 Ophthalmology
014 Radiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L133 ANSWER 22 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-449117 [42] WPIDS
CROSS REFERENCE: 2002-599262 [64]; 2003-210047 [20]; 2003-300471 [29]
DOC. NO. CPI: C2003-119143

TITLE: Lipid constructs useful for treating e.g. cancer, rheumatoid arthritis, psoriasis comprises a linking carrier and a targeting entity.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): PEASE, J S; SHEN, Z M; WARTCHOW, C A
PATENT ASSIGNEE(S): (TARG-N) TARGESOME INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003028643	A2	20030410	(200342)*	EN	29

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003028643	A2	WO 2002-US31090	20021001

PRIORITY APPLN. INFO: US 2001-976254 20011011; US 2001-236310P 20011001

AB WO2003028643 A UPAB: 20030703
NOVELTY - A lipid construct comprises a linking carrier, a targeting entity, and optionally a therapeutic entity.

ACTIVITY - Cytostatic; Antirheumatic; Antiarthritic; Antipsoriatic; Antiinflammatory; Ophthalmological; Antidiabetic; Vulnerary; Antiarteriosclerotic; Dermatological; Antimetastatic; Angiogenetic; Immunosuppressive; Vasotropic; Hemostatic.

An antivascular endothelial growth factor receptor (VEGFR)-2 antibody-dextran-polymerized vesicle-90Y complex (test) (200 micro l) was administered intravenously to mice implanted with K1735-M2 melanoma cells. The control mice were administered with an identical complex not containing dextran. The mean normalized tumor volume was 4 after 8/13 days for the test/control complex respectively.

MECHANISM OF ACTION - None given.

USE - For treating cancer, solid tumors, blood born tumors (e.g. leukemias), tumor metastasis, benign tumors (e.g. hemangiomas, acoustic neuromas, neurofibromas, trachomas, and pyogenic granulomas), rheumatoid arthritis, psoriasis, chronic inflammation, ocular angiogenic diseases (e.g. diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular **glaucoma**, retrolental fibroplasia, rubeosis), arteriovenous malformations, ischemic limb angiogenesis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophilic joints, angiofibroma, wound granulation, intestinal adhesions, atherosclerosis, restenosis, scleroderma and hypertrophic scars (i.e. keloids).

Dwg.0/4

L133 ANSWER 23 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-210047 [20] WPIDS
CROSS REFERENCE: 2002-599262 [64]; 2003-239092 [23]; 2003-300471 [29]; 2003-449117 [42]
DOC. NO. CPI: C2003-053432
TITLE: New targeted macromolecules are cell adhesion inhibitors used for treating e.g. cancer, psoriasis, atherosclerosis

and rheumatoid arthritis comprise linking carrier and targeting entities.

DERWENT CLASS: A96 B05 D16

INVENTOR(S): BEDNARSKI, M D; CHOI, S H; DANTHI, N S; DECHENE, N E; PEASE, J S; SHEN, Z M; TRULSON, J; WARTCHOW, C A; ZHANG, M

PATENT ASSIGNEE(S): (TARG-N) TARGESOME INC

COUNTRY COUNT: 99

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002096367	A2	20021205	(200320)*	EN	65

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002096367	A2	WO 2002-US17191	20020530

PRIORITY APPLN. INFO: US 2001-976254 20011011; US 2001-294309P 20010530; US 2001-309104P 20010731; US 2001-312435P 20010815

AB WO 200296367 A UPAB: 20030703

NOVELTY - New targeted macromolecule (M1) comprises a linking carrier (a) and at least one targeting entity (b).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) new compounds of formula Me-(CH2)11-C triple bond C-C triple bond C-(CH2)8-CONH-CH2-CH2-O-CH2-CH2-O-CH2-CH2-NHCO-CH2-N(Q)-CH2-CH2-N(Q)-CH2-CH2-N(Q)-CH2-CONH-CH2-CH2-O-CH2-CH2-O-CH2-CH2-O-NHCO-(CH2)8-C triple bond C-C triple bond C-(CH2)11-Me (I);

(2) a macromolecule comprising more than one 3-(4-(2-(3,4,5,6-tetrahydropyrimidin-2-ylamino)-ethyloxy)-benzylamino)-2(S)-benzene-sulfonyl-aminopropionic acid group, and

(3) preparation of a targeted therapeutic agent which comprises associating a therapeutic entity within the targeted lipid construct comprising at least one targeting entity.

Q = a group of formula (i).

ACTIVITY - Cytostatic; Antipsoriatic; Antiinflammatory; Antiarthritic; Antirheumatic; Antianginal; Antidiabetic; Ophthalmological; Immunosuppressive; Vasotropic; Antiarteriosclerotic; Dermatological; Vulnerary; Osteopathic.

MECHANISM OF ACTION - Cell adhesion inhibitor.

In a cell adhesion inhibition assay carried out on plates coated with vitronectin, using human melanoma cell line M21, polymerized vesicles (PV) and 3-(4-(2-(3,4,5,6-tetrahydropyrimidin-2-ylamino)-ethyloxy)-benzylamino)-2(S)-benzene-sulfonyl-aminopropionic acid (A) were separately incubated with M21 cells. After 1 hour, cell adherence was measured with crystal violet and optical density was measured at 590 nm. The IC50 values for (A) and PV were 64 mu m and 0.27 mu m, respectively.

USE - Used for targeting different biological targets, where vascular-targeted therapy agent is useful against the vasculature of tumors for treating cancer, solid tumors, blood born tumors (e.g. leukemia, tumor metastasis, benign tumors (e.g. hemangiomas, acoustic neuromas, neurofibromas, trachomas or pyrogenic granulomas), rheumatoid

arthritis, psoriasis, chronic inflammation, ocular angiogenic diseases (e.g. diabetic retinopathy, retinopathy of prematurity, macular degeneration, corneal graft rejection, neovascular **glaucoma**, retrolental fibroplasia or rubeosis), arterivenous malformations, ischemic limb angiogenesis, Ossler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophilic joints, angiofibroma, wound degranulation, internal adhesions, atherosclerosis, restenosis, scleroderma, hypertrophic scars or osteoarthritis. (M1) Are also useful for intracellular delivery of a desired molecule (e.g. a polynucleotide or gene) to the target cell and as imaging agents for imaging, particularly a tumor by magnetic resonance imaging or nuclear scintigraphy.

ADVANTAGE - The stabilizing entity in (M1) provides the capacity for multivalency. (M1) Binds specifically and with high avidity to the biological targets and exhibits upto 200 times increase in their capacity to block cell adhesion, when compared to the monomeric ligands and accumulate in vivo in tumors in a mouse melanoma model. (M1) Complexes with DNA and facilitate the transfer of DNA through cell membrane into the intracellular space of a cell to be transformed with heterologus DNA. (M1) facilitate the release of DNA in the cell cytoplasm, thus increasing gene transfection during gene therapy in humans or animals.

Dwg.0/39

L133 ANSWER 24 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-058516 [05] WPIDS
DOC. NO. CPI: C2003-015011
TITLE: Composition useful for delivering nucleic acid to target cell, comprises admixture of nucleic acid molecule and contrast agent.
DERWENT CLASS: B04 D16
INVENTOR(S): ATALAR, E; YANG, X
PATENT ASSIGNEE(S): (ATAL-I) ATALAR E; (YANG-I) YANG X; (UYJO) UNIV JOHNS HOPKINS
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002081634	A2	20021017	(200305)*	EN	57

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2002192688 A1 20021219 (200306)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002081634	A2	WO 2002-US10697	20020404
US 2002192688	A1 Provisional	US 2001-281589P	20010405
		US 2002-116709	20020404

PRIORITY APPLN. INFO: US 2001-281589P 20010405; US 2002-116709 20020404

AB WO 200281634 A UPAB: 20030121
NOVELTY - A composition (I) comprising an admixture of a nucleic acid molecule and a contrast agent, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a medical access device (II) comprising a housing defining a number of channels, at least one channel having a delivery channel comprising at

least one exit port and at least one channel comprising an inflation channel comprising at least one exit port, a dilation balloon in communication with the at least one exit port of the inflation channel, the dilation balloon comprising at least one perfusion channel, a delivery balloon in communication with the at least one exit port of the delivery channel, the delivery balloon comprising a number of pores.

ACTIVITY - Hypotensive; Antiarteriosclerotic; Anticoagulant; Vasotropic; Cytostatic; Antirheumatic; Antiarthritic; Antiatherosclerotic; Antidiabetic; Ophthalmological.

MECHANISM OF ACTION - Gene therapy; Activator of tissue plasminogen and anchored urokinase; Inhibitor of tissue metalloproteinase; Proliferator of cell nuclear antigen and angiogenic factor; Suppressor of tumor.

No biological data is given.

USE - (I) is useful for delivering a nucleic acid to a target cell, by administering (I) to the target cell. The target cell is selected from heart, liver, prostate, kidney, neural, thyroid, muscle, hematopoietic, circulating, cell of a blood vessel and neoplastic cells. The target cell is part of a multicellular organism. The method further involves detecting a signal which comprises a magnetic resonance signal, associated with the contrast agent. The method further involves localizing the signal to a location in the multicellular organism. Localizing the signal to a location indicates delivery of the nucleic acid molecule to the location. The nucleic acid encodes a gene product necessary for correcting, normalizing, and/or preventing an abnormal physiological response by the target cell. The nucleic acid molecule further comprises a marker gene and the presence of the marker gene in the target cell is determined. The expression of the marker gene is determined. The nucleic acid molecule is encapsulated within a viral capsid. (II) is useful for delivering an agent to a target cell, by positioning (II) in the lumen of a body vessel comprising the target cell, inflating the dilation balloon to compress the walls of the blood vessel, while permitting bodily fluids to flow through the lumen through at least one perfusion channel of the dilation balloon, delivering a solution comprising the agent through the delivery channel to the delivery balloon and from the delivery balloon to at least a portion of an inner wall of the body lumen, through the number of pores in the delivery balloon. The target cell is endothelial cell. The method further involves monitoring delivery of the agent by detecting a signal associated with a contrast molecule, imaging the body vessel, and imaging navigation of the device in the body vessel, where the agent is (I). (All claimed.) (I) is also useful in vascular gene therapy. The gene which is delivered to a target cell is useful to prevent, correct, or normalize or improve, an abnormal condition including hypertension, atherogenesis, thrombosis, intimal hyperplasia, restenosis following angioplasty or stent placement, ischemia, neoplastic diseases (e.g. tumors and tumor metastasis), benign tumors, connective tissue disorders (e.g. rheumatoid arthritis, atherosclerosis), ocular angiogenic diseases (e.g. diabetic retinopathy, macular degeneration, corneal graft rejection, neovascular **glaucoma**), cardiovascular disease, cerebral vascular disease, diabetes-associated disease and immune disorders.

Dwg.0/6

L133 ANSWER 25 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-120400 [11] WPIDS
DOC. NO. NON-CPI: N2003-095986
DOC. NO. CPI: C2003-030992
TITLE: Magnetic resonance imaging composition for imaging cell death in vivo, comprises annexin coupled to contrast agent and radioisotope.
DERWENT CLASS: A89 B04 D16 K08 P31
INVENTOR(S): GREEN, A M
PATENT ASSIGNEE(S): (THES-N) THESEUS IMAGING CORP
COUNTRY COUNT: 100

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002080754	A2	20021017	(200311)*	EN	32

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

US 2002192162 A1 20021219 (200311)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002080754	A2	WO 2002-US10238	20020403
US 2002192162	A1 Provisional	US 2001-281277P	20010403
		US 2002-114927	20020403

PRIORITY APPLN. INFO: US 2001-281277P 20010403; US 2002-114927 20020403

AB WO 200280754 A UPAB: 20030214

NOVELTY - A magnetic resonance imaging composition (I) comprises an annexin coupled to a contrast agent, and optionally with radioisotope.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an optical imaging composition (II) comprising an annexin coupled to an optically active molecule.

ACTIVITY - Ophthalmological. No supporting data is given.

MECHANISM OF ACTION - None given.

USE - (I) is useful for imaging cell death in a mammalian subject in vivo, by administering (I) and obtaining magnetic resonance image, where the image is a representation of cell death in the mammalian subject. (II) is useful for imaging cell death in a mammalian subject in vivo, by administering (II), illuminating the subject with a light source, and visually monitoring the presence of the optical imaging composition in the subject, thus obtaining an image, where the image is a representation of cell death in the mammalian subject. The magnetic resonance image or optical image is obtained between 5 minutes and 2 hours or 12-30 hours after the administration of the magnetic resonance or optical imaging composition. The cell death is caused by **apoptosis**. Imaging further involves obtaining a magnetic resonance or optical image at several time points, thus monitoring changes in the number or location of cells undergoing cell death. The cell death is imaged in an organ (head, brain, heart, liver or eye) of a subject or its portion. (II) is useful in tumor radiotherapy, by administering (II) to a subject bearing a tumor and illuminating the subject with a light source in the presence of oxygen, thus creating a toxic form of oxygen capable of destroying the tumor. The toxic form of oxygen is singlet oxygen. The tumor is a brain tumor, head tumor, neck tumor, breast tumor, esophagus tumor, lung tumor, pleural cavity tumor, ovary tumor, abdominal cavity tumor, bladder tumor, prostate tumor, cervix tumor or skin tumor (all claimed). (I) is useful for determining the extent of **apoptosis** to quantify patients for administering therapeutically modified annexin and for determining the optimal dose of therapeutically modified annexin. (I) is applicable in the field of magnetic affinity chromatography, magnetic cell sorting, or in magnetic immunoassay. (I) is useful for imaging and quantifying **apoptotic** cell death in normal and malignant tissues undergoing treatment. (I) is also useful in monitoring the progress of treatment or the progress of disease, in early detection of certain disease, to track

changes in the intensity of the emission from the subject over time, reflecting changes in the number of cells undergoing cell death, and to track changes in the localization of (I) in the subject over time, reflecting changes in the distribution of cells undergoing cell death. (I) or (II) is useful for detecting inappropriate or insufficient **apoptosis** in disease states, for monitoring **apoptotic** and/or necrotic cell death, organ and bone marrow transplant rejection or injury, infectious and non-infectious inflammatory disease, autoimmune disease, cerebral and myocardial infarction and ischemia, cardiomyopathies, atherosclerative disease, neural and neuromuscular degenerative diseases, sickle cell disease, beta -thalassemia, cancer therapy, acquired immunodeficiency syndrome (AIDS), myelodysplastic syndromes or toxin-induced liver disease, and as clinical research tool to study the normal immune system, embryological development, and immune tolerance and allergy. (I) or (II) is useful in the diagnosis and/or treatment of eye disease such as **retinal** disease or **glaucoma**. Using (I) or (II) the response of individual patients to established therapeutic anti-cancer regimens may be efficiently and timely evaluated, the anti-neoplastic activity of new anti-cancer drugs may be evaluated, the optimal dose and dosing schedules for new anti-cancer drugs may be identified, and the optimal dose and dosing schedules for existing anti-cancer drugs and drug combinations may be identified. Using (I) or (II) the cancer patients in clinical trials is categorized efficiently into responders and non-responders to therapeutic regimens.

ADVANTAGE - (I) allows rapid testing and development of new drugs and therapies in a variety of diseases, and is non-invasive for evaluating the early response of individual patient tumors to chemotherapy.

Dwg.0/2

L133 ANSWER 26 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-616115 [71] WPIDS
DOC. NO. CPI: C2001-184374
TITLE: Delivering anionic agents through lipid membranes includes contacting agent with delivery-enhancing formulation, allowing polyplex to form and contacting lipid membrane with penetration enhancer.
DERWENT CLASS: A96 B07 D16
INVENTOR(S): BANASZCZYK, M; CARLO, A T; CHIOU, H C; LOLLO, C P; MULLEIN, P M; WU, D
PATENT ASSIGNEE(S): (IMMU-N) IMMUNE RESPONSE CORP; (BANA-I) BANASZCZYK M; (CARL-I) CARLO A T; (CHIO-I) CHIOU H C; (LOLL-I) LOLLO C P; (MULL-I) MULLEIN P M; (WUDD-I) WU D
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001060415	A1	20010823	(200171)*	EN	115

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001038485 A 20010827 (200176)
US 2003134420 A1 20030717 (200348)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001060415	A1	WO 2001-US5234	20010216
AU 2001038485	A	AU 2001-38485	20010216

US 2003134420 A1	Provisional	US 2000-183516P	20000218
	Cont of	WO 2001-US5234	20010216
		US 2002-211214	20020802

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001038485 A	Based on	WO 200160415

PRIORITY APPLN. INFO: US 2000-183516P 20000218; US 2002-211214 20020802

AB WO 200160415 A UPAB: 20011203

NOVELTY - Methods for delivering anionic agents through lipid membranes comprise:

(a) contacting the anionic agent with a delivery-enhancing formulation comprising a cationic backbone, a hydrophobic and a hydrophilic group;

(b) allowing a polyplex to form; and

(c) contacting the lipid membrane with a penetration enhancer, so that the anionic agent is delivered upon contact of the polyplex with the lipid membrane.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for polymers poly-L-lysine-graft-(eta -NH-PEG5K)12.8-graft-(epsilon -NH-CH2CONHCH2CH2CH2-O- beta -cholesterol ether)26, PLL10K-graft-(eta -NH-C10-PEG2K)9, PL10K-graft-(eta -NH-C10-Trition X405)9, PL9.4K-graft-(eta -NH-C10-Igepal-CO-990)3.2, PLL9.4K-graft-(eta -NH-Brij700)2.8, PLL9.4K-graft-(eta -NH-C10-Brij700)6.6, PLL9.4K-graft-(eta -NH-CH2CH(OH)(CH2)9-PEG5K)6.5, PLL9.4K-graft-(eta -NH-Brij98)11, PLL9.4K-graft-(eta -NH-Brij98)6, PLL9.4K-graft-(eta -NH-CH2CH(OH)CH2O(PO)61(EO)113OCH3)9.8, PLL9.4K-graft-(eta -NH-CH2CH(OH)CH2O(PO)61(EO)113OCH3)24.6, polyethyleneimine-graft-(NH-CH2CH(OH)CH2O(PO)61(EO)113OCH3)7, polyethyleneimine-graft-(NH-CH2CH(OH)CH2O(PO)61(EO)113OCH3)15, PEG5K-block-(CysC18)10-block-(Lys)45 and PEG5K-block-(CysC18)10-block-(Lys)120.

ACTIVITY - Hepatotrophic; virucide; antiinflammatory; hemostatic; immunosuppressive; vulnerary; vasotropic; antilipemic; neuroprotective; anorectic; antiallergic; antiasthmatic; anticonvulsant; antiparkinsonian; ophthalmological; cytostatic; dermatological.

MECHANISM OF ACTION - Gene therapy.

USE - The methods are used to deliver anionic agents through lipid membranes (claimed) in vivo and in vitro. They are used to enhance expression of nucleic acids in cells (claimed). They are used to treat subjects, including humans, suffering from genetic or acquired disorders such as hepatitis, inflammatory diseases, hemophilia, metabolic deficiencies, metabolic disorders, immune rejection of transplanted tissue, infections by invading pathogens, tissue trauma, ischemia, lipid metabolism disorders cholesterolemia, hypercholesterolemia, peripheral and central nervous system disorders and regeneration, obesity, allergies, allergic rhinitis, asthma, Gaucher's disease, epilepsy, Parkinson's disease, ocular diseases, elevated **intraocular pressure**, cancer, skin disorders and alopecia (claimed).

ADVANTAGE - The methods allow anionic agents to be delivered through lipid membranes (claimed).

Dwg.0/17

L133 ANSWER 27 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-290611 [30] WPIDS
DOC. NO. NON-CPI: N2001-207593
DOC. NO. CPI: C2001-089053
TITLE: Novel urokinase plasminogen activator cell surface receptor-targeting protein or peptide, useful for inhibiting angiogenesis or cell migration, invasion or

proliferation, is diagnostically or therapeutically labeled.

DERWENT CLASS: B04 D16 K08 S03
INVENTOR(S): JONES, T R; MAZAR, A P
PATENT ASSIGNEE(S): (ANGS-N) ANGSTROM PHARM INC
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001025410	A2	20010412	(200130)*	EN	35

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2000079868	A	20010510	(200143)		
EP 1218496	A2	20020703	(200251)	EN	

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001025410	A2	WO 2000-US26502	20000927
AU 2000079868	A	AU 2000-79868	20000927
EP 1218496	A2	EP 2000-970496	20000927
		WO 2000-US26502	20000927

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000079868	A	Based on	WO 200125410
EP 1218496	A2	Based on	WO 200125410

PRIORITY APPLN. INFO: US 1999-157012P 19991001

AB WO 200125410 A UPAB: 20010603

NOVELTY - A urokinase plasminogen activator (uPA) cell surface receptor (uPAR)-targeting protein or peptide (I), is new.

DETAILED DESCRIPTION - A urokinase plasminogen activator (uPA) cell surface receptor (uPAR)-targeting protein or peptide (I), is new. (I):

(a) is diagnostically or therapeutically labeled;

(b) comprises at least 38 amino acid residues;

(c) includes residues 13-30 of the uPAR -binding site of uPA;

(d) competes with labeled isopropyl fluorophosphate (DFP)-uPA for binding to a cell or molecule that has a binding site for uPA;

(e) has an IC50 value of 19 nM or less; and

(f) is not a fusion protein where the uPA peptide is fused to another non-uPA protein or peptide.

INDEPENDENT CLAIMS are also included for the following:

(1) a diagnostically useful uPAR-targeting composition (II) comprising (I) having a detectable label, and a carrier;

(2) a uPA active site-targeting compound (III), preferably a peptide compound that covalently modifies the active site of two-chain uPA (tcuPA), its fragment or subunit, or that binds to the endosite and one or more exosites of tcuPA, its fragment or subunit, where the fragment or subunit retains the uPA enzymatic endosite and a uPAR-binding epitope, (III) covalently modifies the endosite, and comprises a detectable label, a therapeutic moiety, or a chelator that is optionally bound to a detectable label or a therapeutic moiety, (III) localizes the chelator,

detectable label or therapeutic moiety to the uPA active site;

(3) a molecule (IV) comprising (III) bonded covalently to uPA, tcuPA, or its fragment or subunit, where the fragment or subunit retains the uPA enzymatic endosite, and a uPAR-binding epitope;

(4) detecting (M) the presence of uPAR on the surface of a cell, in a tissue, in an organ, or in a biological sample, which cell, tissue, organ or sample is suspected of expressing uPAR due to a pathological state, comprising contacting the cell, tissue, organ or sample with (I), (II), (III) or (IV), and detecting the presence of the label associated with the cell, tissue, organ or sample; and

(5) a diagnostic or therapeutic uPAR-targeting pharmaceutical composition (V), comprising (I), (II), (III), or (IV) to which is bound directly or indirectly a therapeutically active moiety or a detectable label.

ACTIVITY - Cytostatic; antiatherosclerotic; vasotropic; antidiabetic; ophthalmological; antiarthritic; antiulcer; vulnerary.

MECHANISM OF ACTION - Inducer of apoptosis; inhibitor of cell migration, cell invasion, cell proliferation or angiogenesis (claimed).

No biological data is given.

USE - (V) is useful for inducing apoptosis, for inhibiting cell migration, cell invasion (preferably invasiveness of tumor cells), cell proliferation or angiogenesis, and for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis (claimed). (I) is also useful for treating diseases or conditions including primary growth of a solid tumor, leukemia or lymphoma, tumor invasion, metastasis or growth of tumor metastases, atherosclerosis, myocardial angiogenesis, telangiectasia, corneal disease, rubeosis, neovascular **glaucoma**, diabetic and other retinopathy, macular degeneration, arthritis, fibrosis, wound healing with scarring and fibrosis, peptic ulcers, bone fracture, keloids, or a disorder of vasculogenesis, hematopoiesis, ovulation, menstruation, pregnancy or placentation associated with pathogenic cell invasion or with angiogenesis. (I) is useful for hybridization of a fluorescently labeled cDNA probe (fluorescent in situ hybridization (FISH) probe) complementary to uPA or to uPAR mRNA expressed in a tumor and detected in vitro in a paraffin embedded or frozen tissue section derived from the tumor. (I) is useful for diagnosing conditions such as tumors in human or veterinary medicine.

ADVANTAGE - (I) is internalized by the cells to which it binds, e.g. tumor cells, and is useful for imaging techniques in which it reduces the background signal relative to specifically bound probes. This uptake permits clearance of circulating probe so that the ratio of labeled probe inside tumor cells to the probe elsewhere in the body increases.

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L133 ANSWER 28 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-160635 [14] WPIDS
DOC. NO. CPI: C2000-050125
TITLE: New phototherapeutic compounds containing indium.
DERWENT CLASS: B02
INVENTOR(S): PHADKE, A S; ROBINSON, B C
PATENT ASSIGNEE(S): (MIRA-N) MIRAVANT PHARM INC
COUNTRY COUNT: 24
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000000204	A1	20000106	(200014)*	EN	130
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP RU US					
AU 9883794	A	20000117	(200026)		
EP 1091742	A1	20010418	(200123)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

JP 2002519327 W 20020702 (200246) 153
US 6444194 B1 20020903 (200260)
AU 761891 B 20030612 (200349)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000000204	A1		WO 1998-US13601	19980629
AU 9883794	A		AU 1998-83794	19980629
			WO 1998-US13601	19980629
EP 1091742	A1		EP 1998-934216	19980629
			WO 1998-US13601	19980629
JP 2002519327	W		WO 1998-US13601	19980629
			JP 2000-556789	19980629
US 6444194	B1	Cont of	US 1997-801841	19970214
			WO 1998-US13601	19980629
			US 1999-308884	19990526
AU 761891	B		AU 1998-83794	19980629
			WO 1998-US13601	19980629

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9883794	A	Based on	WO 200000204
EP 1091742	A1	Based on	WO 200000204
JP 2002519327	W	Based on	WO 200000204
US 6444194	B1	Based on	WO 200000204
AU 761891	B	Previous Publ.	AU 9883794
		Based on	WO 200000204

PRIORITY APPLN. INFO: WO 1998-US13601 19980629

AB WO 200000204 A UPAB: 20000320

NOVELTY - Phototherapeutic compounds are claimed comprising an atom of In113 or In115 complexed with the inner nitrogens of a pyrrolic core composed of at least 2 pyrroles linked via C or N.

DETAILED DESCRIPTION - Phototherapeutic compounds are claimed comprising an atom of In113 or In115 complexed with the inner nitrogens of a pyrrolic core composed of at least 2 pyrroles linked via C or N. Fully unsaturated porphyrins of formula (I; R1, R2, R4, R6 = Me, R8, R10-R12 = H, R7, R8 = CH2CH2COR13, R13 = amino acid moiety) and (II; R1 = CH(OR)Me, R= alkyl, R2 = amino acid moiety, M = 2H, Ga, Zn, Pd, In or Sn) are excluded (sic).

An INDEPENDENT CLAIM is also included for free bases or metal complexes of formula (III) or (IV).

M = 2H or a metal cation and associated counterion;

R1-R3 = COOH, COOR4, CONR4, CH3Y', CONR4R4, NH2, N(R4)2, N(R4)3+Z- or CONHR6OR7;

R4 = alkyl;

R6 = bivalent moiety comprising n alkylene groups and n-1 oxygens linking two alkylene groups through ether linkage;

R7 = alkylene; X = H, CH=CH2, Et, COOOMe or CHO;

Y = Me or CHO;

Y' = not defined;

provided that the molecular includes at least one R6 group.

ACTIVITY - Antiarteriosclerotic; Vasotropic; Cytostatic; Antipsoriatic; Ophthalmological; Virucide; Antiarthritic; Antirheumatic. Indium methyl pyropheophorbide (IVa) i.e. (IV; M = InCl, X = vinyl, Y = Me, R1 = COOMe) was administered at 0.2 mu mole/kg to the tail vein of 10 C3H/HeJ mice with 5 mm BA mammary carcinomas and 6 or 8 hours later the mice were irradiated with 200 J/cm2 of 75 mW/cm2 light. After 30 days the % cure was 80%.

MECHANISM OF ACTION - Photosensitizer.

USE - As phototherapeutic compounds that absorb light or long wavelengths for use in photodynamic therapy and diagnosis of disease states such as atherosclerosis, restenosis, cancer, cancer precursors, non-cancerous hyperproliferating diseases, psoriasis, macular degeneration, **glaucoma** and viruses, benign prostate hyperplasia and rheumatoid arthritis.

ADVANTAGE - Compounds have improved localization at target site or improved binding to receptors at target area and thus therapy is improved. Dwg.0/0

L133 ANSWER 29 OF 29 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-539590 [45] WPIDS
DOC. NO. CPI: C1999-157626
TITLE: Increasing blood flow in the optic nerve, for the treatment of low tension **glaucoma**.
DERWENT CLASS: B02
INVENTOR(S): MARKSTEIN, R
PATENT ASSIGNEE(S): (SANO) SANDOZ LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5955468	A	19990921	(199945)*		3

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5955468	A	Cont of	US 1994-360159	19941220
			US 1995-466505	19950606

PRIORITY APPLN. INFO: DE 1993-26010U 19931221
AB US 5955468 A UPAB: 19991103
NOVELTY - Increasing blood flow in the optic nerve comprises administration of benzo(g)quinoline derivatives (I), or their hydrolyzable esters, or salts.

DETAILED DESCRIPTION - Increasing blood flow in the optic nerve comprises administration of benzo(g)quinoline derivatives of formula (I), or their hydrolyzable esters, or salts.

Rings A and B are trans-fused;

R1, R2 = H, OH, or OCH3, provided that they are not both H;

R3 = H or 1-4C alkyl;

R4 = COOH, CH2OR5, CH2CN, CONR6R7, CH2SR8, NHSO2NR9R10, or N(H)CONR9R10;

R5, R6 = H or 1-3C alkyl;

R7 = H, 1-3C alkyl or phenyl or pyridyl (optionally substituted by halo, CH3 or OCH3); or

R6+R7 = (CH2)4, (CH2)5, or (CH2)2O(CH2)2;

R8 = 1-4C alkyl, or pyridyl (optionally substituted by halo, CH3 or OCH3); and

R9, R10 = H or 1-3C alkyl; or

R9+R10 = (CH2)4, or (CH2)5.

ACTIVITY - Ophthalmological.

MECHANISM OF ACTION - Increases blood flow to the optic nerve.

In tests, rats were anesthetized with isoflurane and the femoral vein was cannulated for injection if the paramagnetic contrast agent **Gd** (diethylenetriamine pentaacetate). (-)-(3 beta ,4a alpha ,10a beta)-1,2,3,4,4a,5,10,10a-Octahydro-3-((2-pyridylthio)methyl)-1-methyl-6-hydroxy-benzo(g)quinoline (Ia) was administered in amount 0.1 mg/kg, and blood flow was determined by nuclear magnetic resonance (NMR) imaging.

After 30 minutes, (Ia) had improved blood flow in the optic nerve by 30 %, compared to the prior art compound Timolol which did not show any increase in blood flow at 0.5 mg/kg.

USE - The treatment is used for increasing blood flow in the optic nerve, especially for the treatment of low tension **glaucoma** (claimed).

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